UNIVERSITY
OF MICHIGAN
JAN 28 1952
MEDICAL
LIBRARY

BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY JANUARY 5 1952

TABLE OF CONTENTS

Tissue Reactions to Protein Sensitization J. R. SQUIRE, M.D., F.R.C.P. 1

Dental Disease Among 14-year-old London School-children in 1947 and 1950
LADY MELLANBY and HELEN MELLANBY, M.D., Ph.D. 7

Intestinal Macrocytic Anaemia
G. M. WATSON, D.Ph., M.B., M.R.C.P., and L. J. WITTS, M.D., F.R.C.P. 13

Effect on Bleeding-time of an Extract of Blood of Patients with Rheumatoid Arthritis
RAYMOND GREENE, D.M., M.R.C.P., JOSEPHINE VAUGHAN-MORGAN, B.SC., and JULIA GAMMON, B.SC. 17

Sterilization of Woollen Fabrics H. F. BARNARD, M.B., B.S. 21

Bacteriology of Vaginal Flora After Use of Internal Tampons
ELIZABETH N. BRAND, M.D., D.P.H. 24

T-piece Technique for General Inhalational Anaesthesia JOHN BULLOUGH, M.B., D.A. 28

MEDICAL MEMORANDUM
Leukaemia with Primary Gynaecological Manifestations. C. E. W. WHEATON, M.D., M.R.C.P. 30

REFRESHER COURSE
The Painful Shoulder. R. J. W. WITHERS, M.D., M.Ch., F.R.C.S.Ed. 40

GENERAL ARTICLES AND NEWS
Visiting Children in Hospital. ALAN MONCRIEFF, M.D., F.R.C.P., and A. M. WALTON, S.R.N., R.S.C.N., S.C.M. 43
Medical New Year Honours 44
Rotatable Sheath Resectoscope. J. E. SEMPLE, F.R.C.S. 46
THE SERVICES 52
UNIVERSITIES AND COLLEGES 52
MEDICAL NEWS 55
BIRTHS, MARRIAGES, AND DEATHS 57

REVIEWS
The Beginning of Life 32
Bleuler on Schizophrenia 32
Coeliac Disease 32
U.S. Public Health Services 33
Books Received 33

MEDICO-LEGAL
Divorce for Incurable Insanity 52

Vital Statistics 53

LEADING ARTICLES
Lung Resection for Pulmonary Tuberculosis 34
House Dust as an Allergen 35

ANNOTATIONS
Specific Language Disability 36
Choice of Antibiotic for Pneumonia 37
Nutrition in New Guinea 37
Compulsory Retirement 38
Winter Epidemics 38
Salmonella minnesota Infection 38
Steroid Metabolism in Idiopathic Hirsutism 39
Family Doctor 39

REPORTS OF SOCIETIES
ROYAL SOCIETY OF MEDICINE: Criminal Responsibility 45

QUESTIONS AND COMMENTS
Seasickness—Molluscum Contagiosum—Safe Period — Chronic Paronychia — Calciferol and Boeck's Sarcoidosis—Toxic Reactions to P.A.S. — Anticoagulants and Cerebral Thrombosis—Adrenal Ascorbic Acid 57-8

SUPPLEMENT
For Contents see First Page of Supplement

CORRESPONDENCE
Death on the Roads. Sir SYDNEY SMITH, M.D.; L. C. NICKOLLS, M.Sc.; TREVOR HUGHES, L.R.C.P.Ed. 47
Fantus Estimation of Urinary Chloride. B. E. COHEN, M.B., and others 48
Hip Reconstruction by Acrylic Prosthesis. G. N GOLDEN, F.R.C.S. 48
Pre- and Post-operative Treatment of Dehydration. J. MIDDLETON PRICE, M.B. 48
Shortage of *X*-ray Film. PETER W. EDWARDS, M.B., and R. L. MIDGLEY, M.D. 49
Exophthalmos. V. C. MEDVEI, M.D. 49
Post-leucotomy Anxiety. F. T. THORPE, M.R.C.S. 49
Invite Russian Doctors. JOHN MCFIE, M.D.; A. W. LIPMANN KESSEL, F.R.C.S. 50
The Doctor and the Courts. E. F. HUNT, M.R.C.S. 50
Criminal Responsibility. C. G. LEAROYD, M.R.C.S. 50

OBITUARY
A. Garrick Wilson, M.Chir., F.R.C.S. 51
N. Mootatamby, L.M.S. 51
Ludolph Brauer, M.D. 51
L. R. J. Rinkel, M.R.C.S. 51
T. L. Gordon, M.B., F.R.C.S.Ed. 52

No. 4748, WEEKLY, PRICE 2/-

Copyright

REGISTERED AS A NEWSPAPER

Pre-Natal Diet and the course of Pregnancy

The normal functioning of the reproductive organs during pregnancy depends, among other things, upon the plentiful intake of vitamins and minerals.

Medical opinion is gaining ground that there is an increased need for Vitamin B in late pregnancy and the early puerperium. Its administration during the period before childbirth has resulted in less vomiting and nausea and in marked improvement in the nutritional value of the breast milk. In order to assure the building of the foetal bones *in utero* and afterwards during breast-feeding, the importance of Vitamin D and of calcium and phosphorus is also established.

In Supavite Capsules the practitioner has at hand a combination of these and other essential vitamins and minerals in a scientifically balanced form of particular value in maternity cases.

Angiers
SUPAVITE
CAPSULES

FORMULA		Each BLACK Capsule contains:	
Each AMBER Capsule contains:		Vitamin B_1	1 mg.
Vitamin A	6,000 I.U.	Vitamin B_2 (Riboflavin)	1 mg.
Vitamin D	1,000 I.U.	Vitamin C	25 mg.
Vitamin E	1 mg. plus one minim wheat germ oil.	Nicotinamide	10 mg.
		Iron (Ferrous)	17 mg.
		Calcium	30 mg.
		Phosphorus	30 mg.

THE ANGIER CHEMICAL CO. LTD., 86, CLERKENWELL ROAD, LONDON, E.C.1

SURGICAL SERVICE SALTAIR

SALT & SON LTD. — for —

SURGICAL BELTS and CORSETS to individual measurements
ELASTIC HOSIERY in all Thread Elastic qualities
TRUSSES for all types of hernia, to individual requirements
ORTHOPAEDIC APPLIANCES
ARTIFICIAL LIMBS, etc., etc.

An Invitation

Our services are available free of charge to the Medical Profession in carrying out work of an experimental nature for any new type of surgical support.

LONDON ADDRESS FOR APPOINTMENTS:—
1, STANLEY HOUSE, 103, MARYLEBONE HIGH ST., LONDON, W.1. TEL. WELBECK 3034.

HEAD OFFICES:
BIRMINGHAM, 2

To assist convalescence

Invalid Bovril is a highly concentrated form of Bovril for use in the sick-room. Prepared without seasoning, it provides the maximum concentration in the most easily assimilated form. Many doctors recommend it in cases where the patient needs "building-up" after illness. Perhaps there is a patient of yours who would benefit from a course of Invalid Bovril?

Invalid
BOVRIL
THE ESSENCE OF CONVALESCENCE
SOLD BY ALL CHEMISTS

AN APPROVED METHOD OF *Family Planning*

(included in the approved list of contraceptives issued by The Family Planning Association)

For social and economic reasons medical advice is now being sought more than ever before, on the subject of "PLANNED PARENTHOOD" and Birth Control in its clinical aspect is rapidly becoming a specialised branch of Medical Science. GYNOMIN is spermicidally efficient, clean in application and harmless to health. It is non-irritant, non-greasy and keeps perfectly in all climates.

GYNOMIN

The Scientifically Balanced, Antiseptic and Deodorant Contraceptive Tablet

FORMULA: Each tablet weighs 1.2 gms. and contains w/w: Sodii Bicarb. B.P. 12.7%, Acid Tartaric B.P. 11.1%, Sodium p-toluenesulphonchloroamide B.P. 1.1%, Perfume q.s. Excipients to 100%.

For maximum safety it is advised that Gynomin be used in conjunction with a mechanical barrier.

Samples and medical literature sent on request.

Manufactured by
COATES & COOPER LTD
PYRAMID WORKS
WEST DRAYTON MIDDLESEX

Medical Saxon

BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 5 1952

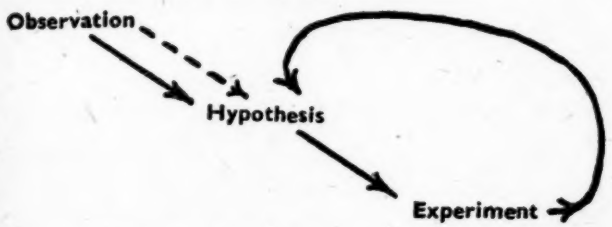
TISSUE REACTIONS TO PROTEIN SENSITIZATION*

BY

J. R. SQUIRE, M.D., F.R.C.P.

Leith Professor of Experimental Pathology, University of Birmingham

As this account is in no way intended to be exhaustive, but rather to illustrate the scientific basis of medicine in one field, it will not be out of place briefly to consider the nature of the processes by which science is built. They may be represented diagrammatically:



The starting-point has always been an observation, usually made in the midst of some practical performance —in medicine, when caring for a patient or examining his body after death. This clinical observation (often associated with others made previously) leads to the formulation of a hypothesis on how the events happened or what was the relation between one observation and another. In scientific medicine such hypotheses are tested by experiment, an attempt being made to reproduce the events observed at will or to replace them by some other event. The success or failure of these efforts leads on to fresh modified hypotheses—sometimes also modified by further observations—and so the cycle goes on. Increasingly, knowledge based on facts replaces speculation.

Much has been written about the nature both of observations and of experiments, good and bad, and there is still much to be learned about these aspects of scientific method. Rather less attention has been paid to the scientific hypothesis. Here only two points can be stressed. In the first place, every effort should be made to keep separate in one's mind the facts of observation and experiment from the theory or hypothesis. This is more easily said than done, for even the description of a fact may lead to hypothetical ideas slipped in with the very words used. Secondly, the distinguishing feature of a good hypothesis is its usefulness, perhaps even more than its ultimate truth. Useful hypotheses are precise and point to crucial experiments which can be performed with the resources available. The remarkable success of most outstanding men of science—and clinical science is no exception — has been due in no small part to their flair for formulating the relevant and right hypothesis at the right time.

To illustrate this scientific basis of medicine in the field of protein sensitization we should try to proceed always from observations on man rather than on animals, and from the "known" (or relatively well understood) phenomena to the "unknown" (or more obscure). With this in mind, I propose to discuss two groups of reactions only, those of the *asthma–hay-fever–urticaria* type, and those showing reactions of the *tuberculin–trichophytin* type. Together they include a wide range of diseases and disease processes. They omit types of reaction of great interest, such as serum sickness or homograft reactions—although a good scientific basis has now been established for discussing the nature of these processes. It is also necessary to omit many disordered functions classified to-day as rheumatic fever, polyarteritis nodosa, etc.—a less serious omission, since we are still not on sure ground in regarding these as examples of protein sensitization reactions, however suggestive one may think the evidence.

Asthma–Hay-fever–Urticaria Group

The first clinical observations linking asthma with sensitization were made by Hyde Salter, of London, and published in a monograph in 1860, "animal emanations" being blamed for the sufferings of many of his patients. Hay-fever had been accurately described some 30 to 40 years previously. In 1873 Blackley, a Manchester practitioner, published his *Experimental Researches on the Causes and Nature of Catarrhus Aestivus* (*Hay-fever or Hay-asthma*), a book of such clarity and method that it should be studied to-day by anyone intending to work in this field. Like many others who have investigated this group of disorders, Blackley himself suffered with severe hay-fever. By testing his own skin he showed that reactions could be induced by some of the agents suspected of eliciting the symptoms in his nose and bronchi. He was thus able to examine current hypotheses, such as the causative effects of dust as such. Road dust from various sources rubbed into scarified skin produced no reaction, but pollen of certain kinds resulted within a few minutes in the now familiar sequence of events, with local swelling as a prominent feature.

*Lecture given to the Postgraduate Medical School and Institute of the British Postgraduate Medical Federation as part of the course on "The Scientific Basis of Medicine." Delivered at the London School of Hygiene on February 27, 1951.

Blackley's skin tests on himself might to-day be regarded as somewhat heroic in dosage, for he describes reactions lasting 24 hours or more, equalling an egg in size; at all events, he obtained results differing considerably from his controls. He was able in this way to define two basic facts about the tissue reactions to protein sensitization of the hay-fever type: (1) the reactions could be reproduced from a number of tissues—the skin of many areas, the conjunctiva, the linings of the nose and bronchi; (2) the reactions were narrowly specific. In his own case strongly positive results were given by the pollens of grasses and of another monocotyledon, the iris. Negative results were obtained with pollens from other (dicotyledonous) flowers. Even more striking examples of specificity have been given later, by examples such as that of a child sensitive to horses but able to ride a donkey in comfort. Blackley's hypotheses were naturally not all correct: obsessed somewhat with his own observations on grass pollens, he speculated about those patients suffering with asthma from animal emanations, pointing out that most of the animals concerned tended to be closely connected with hay—the kind of "association" pitfall which no doubt is trapping all of us to-day in other clinical ideas.

Nature of Skin Reactions

The nature of the skin reactions to protein substances causing asthma and hay-fever is now comparatively well understood. The local reddening and oedema with the surrounding flare—the triple response—were analysed by Sir Thomas Lewis (1927) in a familiar series of experiments of great beauty. The use of histamine to excite closely similar reactions led to the idea of a local release of a diffusible poison or H-substance, with effects limited to the blood vessels. Close comparison of the response to histamine and to protein antigens in suitable subjects by Hare (1926) showed that the two reactions were practically indistinguishable except perhaps for slight delay at the protein site. Similar local oedema and reddening occur in the conjunctiva and mucous membrane of the nose. By analogy with animal anaphylaxis, smooth-muscle contraction has been considered as an additional basis for the reactions of the bronchi in asthma, although it is not known certainly if this occurs in man.* d'Abreu (1940) has described an asthmatic reaction viewed through the bronchoscope: certainly, the reduction of the bronchial lumen was rapid and intense.

The local outpouring of secretions from nasal and bronchial mucous membrane in asthmatic and hay-fever attacks is not fully understood in terms of H-substance reactions. The two salient features of this type of reaction in any tissue are the rapid onset of oedema—within five minutes—and the minimal changes detectable by histological methods. Necrosis, for example, is never found even after considerable local dosage of sensitizing protein. Cellular infiltration, except on occasion for some local eosinophilia, is likewise absent.

The general rule that scientific observations and experiments in any field, initially qualitative, are found to be more rewarding when brought on to a quantitative basis can be illustrated here. If the ordinary prick test is performed with histamine as a test substance the errors of the method and the dose–response relationship can be worked out (Squire, 1950). Modern statistical techniques lighten the labour and extract the maximum information from the results. The prick test, carefully performed, can be shown to have a coefficient of variation (an "error") of not more than 20% for dosages resulting in wheal sizes of 1–6 mm. diameter, provided that standard and comparison tests are made on symmetrically placed sites, left and right, and within a short time of one another. Further errors are introduced if comparisons without standards are made on different days or on different sites (even, say, a few inches further down a forearm).

The diameter of the wheal responses is roughly proportional to the logarithm of the concentration of histamine (or of protein in a sensitive subject). In other words, if the wheal diameter is increased 1–1.5 mm. by raising the strength of the solution from 1:100,000 to 1:10,000 a similar further increase in size will be found by using a solution 10 times stronger still. The amount of solution introduced by a standard "prick"—forcible enough to cause momentary pain, but insufficient to draw blood—can be shown to be about 3 millionths of a millilitre.

From such quantitative considerations it can be shown that tissue reactions are produced by very small amounts of protein in asthmatic patients. A wheal 3 mm. across can be produced, for example, by as little as 10^{-13} g. of horse dandruff protein (probably as little as 10,000 molecules of protein). Similar responses in such a patient were only obtained with histamine solutions weight for weight 1,000 times stronger. As the molecular weight of the dandruff protein is probably 1,000 times as great as that of histamine, we must suppose (if histamine is indeed the reaction-mediating H-substance) that each molecule of dandruff protein introduced into the skin of certain asthmatics liberates (and that within half a minute) about one million molecules of histamine. This hypothesis perhaps needs re-examination. At all events, quantitative skin testing, with standard histamine to check the skin's reactivity and saline controls to avoid errors due to dermatographia, as well as with test protein solutions of known concentration suspected to be responsible for protein sensitization in any given patient, is still a rewarding field for further experiment.

Transfer of Sensitivity

Apart from specific reactions to certain foreign proteins widely disseminated through the body, the tissues of asthmatic patients show no obvious abnormality. Their skins are not, for example, in any way abnormally sensitive to histamine or to other known pharmacologically active bases. The serum or plasma of such patients is abnormal, however, in that, transferred to the body of a normal person, it induces exactly similar specific sensitivity. Clinical observations again gave the lead when Ramirez (1919) observed that blood transfusion from an asthmatic donor resulted in a sensitized recipient. Loveless (1941) made this the basis of experimental observations, showing that the induced sensitivity affected skin, conjunctiva, and mucous membranes, being fully established within 24 hours and lasting, though waning in degree, over periods as long as 30 days.

The local transfer of sensitivity to a small area of normal skin by means of an intradermal injection of, say, 0.05 ml. of asthmatic serum (Prausnitz–Küstner technique) has been widely used and is of practical and theoretical importance. The "antibody" from the

*But see Schild, H. O., Hawkins, D. F., Mongar, J. L., and Herxheimer, H., *Lancet*, 1951, 2, 376.

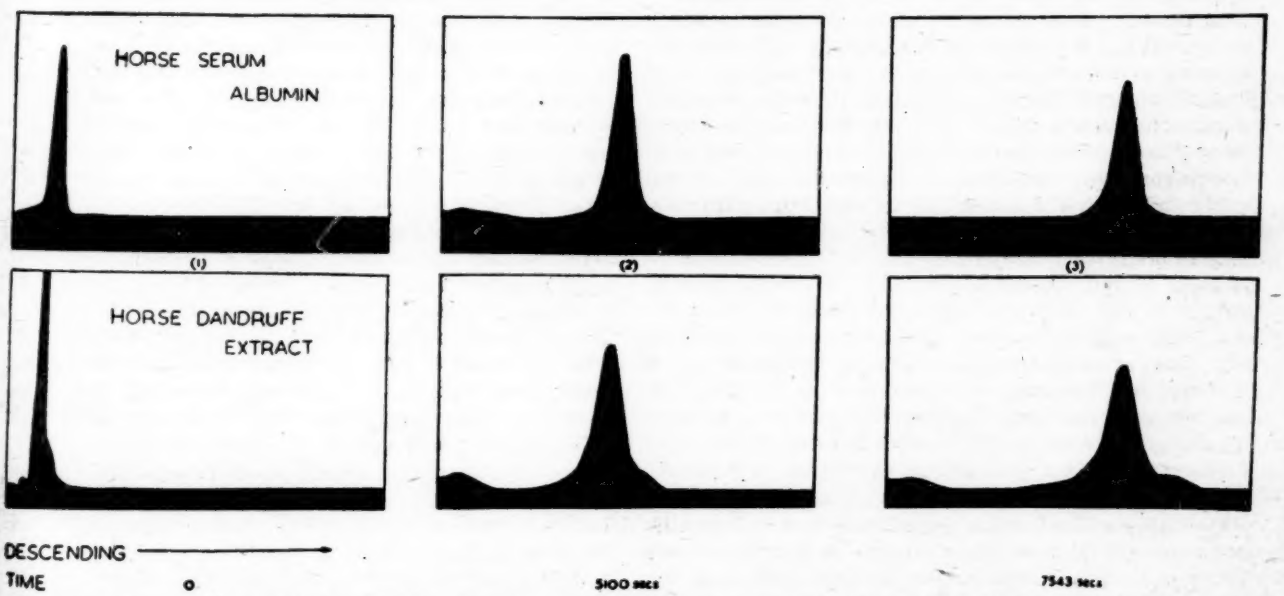
patient is to some extent "fixed" locally, for such a sensitized site is capable of reacting, even if testing is deferred for several days. In particular, this kind of experiment can serve as the basis of a quantitative assessment of sensitizing antibody circulating in the plasma of an asthmatic or hay-fever patient. For a sensitized site, having once given a full reaction, is "discharged" and cannot again be caused to react, even with much stronger test doses of sensitizing protein. This discharging reaction can be obtained either by pricking the sensitized site after, say, 24 hours, or by mixing sensitizing proteins in graded dilutions with the asthmatic serum before introducing it to the normal skin test sites.

If the minimal quantity of sensitizing protein required fully to discharge a site treated with a known quantity of asthmatic serum is regarded as an "equivalence dose" at least, comparative indications are obtained of the amounts of sensitizing antibody per millilitre of any patient's serum. Most immunological reactions—for example, precipitin reactions—involve not very dissimilar numbers of molecules of antigen and antibody. If these passive transfer reactions are assumed to follow a similar pattern, then it seems that quite small amounts of sensitizing antibody—for example, less than 1 mg./ml. of serum—are involved even in highly sensitized asthmatic patients.

Generalizations on Foreign Proteins

Turning to the foreign proteins responsible for tissue reactions in sensitization of the asthma–hay-fever type, certain tentative generalizations are now possible. Those adequately studied—for example, the proteins in grass pollen (Harley, 1937), ragweed pollen (Stull *et al.*, 1931), house-dust (Rimington *et al.*, 1947), and horse dandruff (Squire, 1950)—are all of the general nature of albumins. They are digested by pepsin in acid solution and lose their power to provoke reactions. They are precipitated from solution by saturation with ammonium sulphate, but not by half-saturation. My colleague, Mr. D. R. Stanworth, has been studying horse-dandruff albumin in parallel with recrystallized horse-serum albumin (both of these proteins often giving reactions in patients and suitably immunized animals). The electrophoretic mobility of the main component of the unpurified dandruff albumin closely resembles that of serum albumin in barbitone buffer (see illustration). This general similarity between the proteins sensitizing man by inhalation as dusts is perhaps not extraordinary, being related probably to their molecular size. In general, very small molecules are not potent antigens, while large protein molecules withstand drying poorly, usually being denatured and rendered insoluble. Perhaps, too, large molecules would fail to penetrate the mucous membranes, and so never have an opportunity to sensitize anyone. Guesses of this kind may indicate why the proteins concerned are all found among the "medium-sized" proteins. There is no evidence that they are otherwise related, and they seem to vary considerably in chemical composition—for example, in combined carbohydrate content.

The proteins known to cause sensitization in man are fully antigenic in animals. Precipitins are formed in response to injection, and animals such as guinea-pigs become sensitive, developing anaphylaxis when re-exposed after suitable intervals. Sensitization and shock can be induced, as shown by Ratner (1939), by letting animals inhale a fine spray of dust of such proteins. Sensitization in man can be assumed to follow absorption of the proteins either by inhalation or by ingestion. Direct evidence is lacking, but previous exposure as a cause is strongly suggested by the absence of specific sensitivity (even when sought) in areas of the world which are free from some special protein—for example, that of ragweed pollen in Europe (see Cooke and Sherman, 1950). Normal persons can absorb proteins through the gut, intact enough at least to excite reactions in passively sensitized sites. Lewis used to describe an experiment which failed—but succeeded in a different sense. He had sensitized a site on his forearm with some serum from a fish-sensitive subject, intending to test some preparations of protein by pricking them into the site next day. On leaving his home in the morning, however, he felt his forearm itching, and realized that a reaction had occurred



Comparison between electrophoretic mobilities of horse-serum albumin and horse-dandruff proteins. (Barbitone buffer *p*H 8.6, $\mu/2$ =0.1.) Note that main component of dandruff resembles serum albumin, but that a minor component of greater mobility is also present in dandruff. (Electrophoresis conducted by Mr. D. R. Stanworth.)

prematurely. Unthinkingly, Lewis had accepted and eaten a kipper served for his breakfast (see Lewis and Grant, 1926).

The riddle of asthma, then, is not so much, How can a patient have been sensitized? as, Why are we not all sensitized? Our food, the very air we breathe, is charged with proteins capable of sensitization, and normal individuals absorb these proteins, at least to some extent. True, hay-fever of mild degree is a very common disorder, but well-marked asthma due to protein sensitization in otherwise healthy young persons is not so common. The riddle of the familial tendency to develop sensitization of this degree is still unsolved. Perhaps it implies that intact proteins are more freely absorbed by subjects who are liable to sensitization, though so far no evidence in favour of this idea has been presented. The careful quantitative studies now being conducted in animals to establish the dosage-response relationships between foreign proteins and anaphylactic sensitivity (Kabat, 1947; Coulson and Stevens, 1949) may offer fresh clues and suggest new experiments to be conducted on suitable patients.

Blood Eosinophilia

A feature commonly found in patients of the asthma–hay-fever–urticaria group is a blood eosinophilia. Repeated injections of protein, though each may be temporarily followed by a drop in blood eosinophils, induces eosinophilia in animals (Biggart, 1932). Many observations, but comparatively few experiments, are reported which could help to establish the significance and function of the eosinophil cell. The asthmatic patient's sternal marrow may show slight evidence of increased eosinophil production. If such a patient is kept free from exposure to the proteins to which he is sensitive (for example, in hospital) a gradual decline, say from 600–700 to 300 eosinophils per c.mm., over a period of about six weeks occurs (unpublished observations on a single patient). Such studies have been made reasonably accurate by the direct counting methods of eosinophil cells (Discombe, 1946).

In man and in animals, sensitized tissues affected by exposure to the appropriate foreign proteins may become crowded with eosinophil cells some hours later. As a working hypothesis, the eosinophil cell may be regarded as being concerned with "mopping-up" the products of tissue damage. Certainly, the large granules, so refractile under dark-ground illumination, so dense under phase-contrast microscopy, have some very specific function. In thin films of blood examined when warm and fresh the eosinophil is just about as active as a neutrophil polymorph leucocyte, moving with all its granules (except one or two) foremost. Phagocytosis of cocci by eosinophils is not readily observed in contrast with the behaviour of the polymorph. But the eosinophils will adhere to wettable surfaces, and on occasion—when offered, for instance, clumps of dead tubercle bacilli—they will lie close with only the granules in movement, circulating internally as if allowing different granules a period of active absorption close to the cell surface followed by a period of recovery deep in the cell body.

Are the granules acid (and avid for eosin) and capable of adsorbing base? Apparently, disruption of the eosinophil is the main source of histamine from the cells of the blood (Code, 1937). We are close to confusing fact and hypothesis in this account, but at least it can be said that the eosinophil cell is worthy of greater attention. Easily distinguished and handled as a living cell, its granules appear intact if the cell is disrupted by pressure—they could be separated and analysed.

Tuberculin–Trichophytin Group

The reactions to tuberculin have occupied the attention of physicians ever since Koch (1890) made the unfortunate claim for this substance as a remedy for tuberculosis. It is now clear that sensitization closely analogous to that which follows infection with tubercle bacilli may occur with other infections—for example, by species of the fungus *Trichophyton*, as in athlete's foot. As the details of tuberculin sensitization have been more fully studied, it seems best to concentrate upon these reactions which serve as a type for the whole group. Much space in Arnold Rich's (1944) absorbing book is given over to describing the facts of sensitization. Here only the salient features can be mentioned, with particular stress on the similarities and differences between asthma-type and tuberculin-type sensitizations.

The quality of specificity of the tuberculin reaction is just as striking as that of the asthma–hay-fever group. In fact, the practical application of this form of sensitization at present is in diagnostic tests, which determine whether or not an individual has been infected with tuberculosis. Just as in hay-fever the skin can be shown to be sensitive to many species of grass, so in patients infected with either human or bovine strains of bacilli skin reactions to any tuberculin can be demonstrated. Unrelated infections, however, as with *Trichophyton*, confer sensitization specifically, to, say, trichophytin, and not at all to tuberculin.

Sensitization of the tuberculin type can be shown to be widespread throughout the body, to a greater extent even than in asthma-type sensitization. Lung, kidney, testes, meninges, cornea—all show evidence of sensitization when tested experimentally (see Rich, 1944). The skin has been studied most, as it is most easily observed. When compared with the wheal-reaction characteristic of asthma-type skin tests, the tuberculin reaction differs profoundly even on naked-eye observation. Most striking is the difference in time relations. The mild asthma-type reaction appears in a matter of minutes and fades in half an hour. The tuberculin reaction may just be evident some eight hours after the introduction of the test solution, is at its height after 24 hours, and disappears only after some two to three days. Even then signs of the reaction may persist in the form of slight pigmentation and some flaking of the epidermis, for lasting cytological changes are present in the dermis. Overdosage with tuberculin causes local necrosis, never seen with the skin tests for asthma. Systemic reactions, too, may occur, but again these differ from those following overdosage with the agents which elicit asthma and urticaria, by being slower in onset and more long-lasting, with fever and a general bodily disturbance.

Dosage-response relationships have been worked out with tuberculin as with asthma-type reactions (Wadley, 1949; Long and Miles, 1950). A convenient index of reaction strength is again the diameter of the local oedematous area, but in this case measured after 24 hours rather than after 10–15 minutes. The diameter of the local lesion is also proportional over a fair range to the logarithm of the dose of tuberculin introduced.

Histological Changes

The histological changes accompanying the tuberculin reaction have been described and debated in detail. There can be no doubt about the striking degree of these changes, in contrast with the asthma-type reactions, nor about the extensive cellular infiltration with the various types of wandering cell, including polymorphs and mononuclears, as seen in many kinds of inflammation. Histological examination of lesions is in this case more delicate than clinical observation, in the sense that changes can be seen in sections of skin removed from tuberculin-test sites before the reactions are visible to the naked eye.

The observation that wandering cells participate in these reactions falls into line with the later experimental findings that tuberculin sensitivity can be passively transferred from one individual to another, not as in the Prausnitz–Küstner technique by serum, but only by the transfer of cells (leucocytes). This striking advance was achieved by Chase in 1945. Guinea-pigs were artificially sensitized by injection of tubercle bacilli. When concentrated suspensions of their leucocytes (0.2 ml.) were introduced into normal animals by intravenous or intraperitoneal injection the recipients were clearly sensitized as judged by tuberculin skin-testing, albeit for a few days only. These experiments have been amply confirmed by other workers in the United States, and extended by the work of Lawrence (1949), who showed that more striking degrees of sensitization can be induced in man. Lawrence used relatively smaller dosages of leucocytes, but the human cell donors were probably more highly sensitive than Chase's animals, being selected from patients naturally infected with tuberculosis. The tuberculin-negative recipients were injected intradermally. Sensitization then spread in many instances to involve even remote skin sites, and lasted sometimes for a month or two as judged by the usual intradermal tuberculin tests.

The importance of the motile cells in tuberculin sensitization is also underlined by tissue-culture experiments. The experiments of Rich and Lewis reported in 1932 can justly be described as classical, if not on grounds of antiquity then on the basis of their elegance. In suitable concentrations tuberculin gave no appreciable effect when added to cells grown from tissues of normal guinea-pigs, even if serum from sensitive animals was also added. But cells from guinea-pigs previously sensitized, even when washed and cultured in normal guinea-pig serum, were damaged by similar concentrations of tuberculin. Fibroblasts perhaps were relatively unharmed, but wandering mononuclears migrating out in tissue culture were slowed down, stopped, and eventually killed. Recently, Cruickshank (1951) has extended the idea that not all types of cell from sensitized animals are susceptible to tuberculin, by showing that sensitized guinea-pig epidermis can grow in media containing concentrations of tuberculin considerably above those required to excite gross reactions in the skin of the intact donor animal.

The generalization that tuberculin sensitivity is not dependent upon a serum factor is not disturbed by the experiments of Miller and Favour (1951). These workers have demonstrated that further complexities may be found in the serum of patients in certain stages of tuberculosis, as judged by acute behaviour changes in various blood leucocytes when acted upon by serum-tuberculin mixtures (Favour *et al.*, 1949).

Whereas a special study of the eosinophil leucocyte is needed to increase our knowledge of the asthma–urticaria type of sensitization, with regard to the tuberculin-trichophytin reactions the focus narrows on to the lymphocyte—or at least to the various types of mononuclear cell. These cells are very active in tissues, wandering rapidly from site to site, as described by Ebert *et al.* (1940) in the rabbit's ear.

The chemical eliciting the tuberculin reaction is undoubtedly protein in nature. The work of Seibert (1944) and others has shown that activity can be demonstrated in proteins of various sizes, but that the most highly active material, now usually known as P.P.D. (purified protein derivative) has a molecular weight of about 35,000, and is homogeneous in electrophoretic experiments. The material of lower molecular weight found in old tuberculin is presumably derived from P.P.D. by breakdown. But none of these protein fractions, injected alone by any route, has been shown to cause the development of tuberculin sensitization—another point of major difference from the anaphylactic form of sensitization. But even dead tubercle bacilli, injected in sufficient quantities, readily induce sensitization in suitable animals, such as rabbits and guinea-pigs. It has now been shown that the essential difference between the bacillus and the protein derived from it depends upon the presence of specific materials (perhaps capable of inducing phagocytosis by mononuclear cells), since suitable mixtures of tuberculoprotein with the wax of the tubercle bacillus injected into guinea-pigs have proved capable of inducing specific tuberculin-type sensitivity (see Raffel, 1948). Much remains to be discovered about the differing forms and degrees of sensitization which follow inoculations by different routes and in different mixtures with poorly soluble materials, though striking progress has recently been made, most clearly described (at the same time with a suitable sense of excitement) by Burnet and Fenner (1949).

Control of Sensitivity Reactions

The medical scientist is sometimes, not unjustly, accused of being less interested in the treatment of disease than in the original condition and its basis. This should not be so; not only does the understanding of disease mechanisms suggest rational lines of treatment, but the success or failure of therapy, rational or empirical, may often be used to validate or disprove current theories about the nature of a disease. From this point of view, three methods now in use for controlling the reactions to sensitization merit discussion—"desensitization," the "antihistamine" drugs, and cortisone.

Desensitization

This term was used to describe the effects of sublethal anaphylactic shock in experimental animals. After administration of suitable doses of specific protein, further injections may be without effect or may produce only minor reactions. This state of reduced reactivity, however, lasts only a few days at most; the only parallel in human medicine is probably found in such circumstances as when a horse-sensitive subject is treated with increasing doses of horse serum (starting with very small amounts) during a period of hours, so as to enable an adequate dose of some vitally needed antiserum to be administered. As in the animal, this desensitization is of limited duration.

On the other hand, a course of injections of, say, pollen extracts given to a patient regularly attacked by summer hay-fever, in increasing dosage at intervals of three to seven days, is well known to induce in a fair proportion of instances a gradual lessening of reactivity of skin and other sites to pollen tests and of the symptoms and signs of attacks. Several months of treatment are usually required, and the beneficial results may not last for more than one season.

The confusion of thought resulting from the use of the same word "desensitization" to describe these events has been unfortunate. The procedure required clearly suggests that some form of immunization process is involved, and experiments with the serum from patients treated in this way has confirmed the presence of a neutralizing antibody capable of combining specifically with the pollen protein in such a way that it no longer elicits skin reactions (Loveless, 1940; Harley, 1942). Simple tests—for example, stability to heat—can be used to differentiate this neutralizing antibody from the sensitizing substance originally present in the hay-fever subject's serum. These important findings deserve further work, directed, in particular, towards easier methods of determining *in vitro* the concentration of neutralizing antibody achieved at various stages of this form of treatment. The gradual reduction of tuberculin sensitivity which can be achieved by successive injections of the appropriate protein has not, apparently, been tested to determine whether a similar or different mechanism is involved.

Antihistamine Drugs

These were originally discovered by Bovet and Staub (1937) in Paris. Halpern (1950) has reviewed his own and other contributions to the introduction of compounds suitable for human administration, and has summarized recent experimental work. The antihistamine drugs are usually strikingly effective in controlling urticaria and hay-fever. Caution must be exercised, however, in drawing conclusions from this finding, since only some of these drugs single out histamine for antagonism (see Gaddum, 1948). Quantitative skin-testing shows that a great reduction occurs in the wheal-like responses to specific protein inoculation. Guinea-pig lung reactions to histamine, and (in sensitized animals) to doses of protein considerably greater than those known to cause death in unprotected animals, are abolished. In man, control of asthma is less certain; in some trials the patients' reports of improvement may have been vitiated by insufficient control of the "suggestion" factor—for example, failure to use dummy tablets—in others, the selection of patients has not been such as to ensure that true examples of sensitization were being studied. Whereas the asthma–urticaria group of patients are usually benefited by treatment with the antihistamine drugs, the sensitivity reactions of the tuberculin-trichophytin group are unaffected.

Cortisone

The effects of cortisone and of cortisone-liberating A.C.T.H. have been studied for too short a time for the formulation of more than tentative conclusions. It seems generally agreed at present that these drugs greatly diminish the naked-eye reactions to tuberculin, but have negligible effect on the wheal-like reactions to histamine or to agents such as pollen concerned with the asthma–urticaria type of response. It is clearly of very great importance to study the nature of this inhibition of the tuberculin reaction. A local effect of cortisone on ground-substance of subcutaneous tissue can be demonstrated by measuring dye-spreading round the site of injection (Gell and Hinde, personal communication). Histological studies of tuberculin reactions at various stages in their development in the rabbit have shown a highly significant reduction in the proportion of mononuclear cells as compared with polymorphonuclear leucocytes (Gell and Hinde). Whether these and the various other known effects of these hormones can eventually be correlated into a simple picture is uncertain at present: in their effects on the tuberculin reaction, at least, it seems that once again the behaviour of the mononuclear wandering cell is of major importance.

Conclusions

The study of sensitization often seems to raise as many questions as answers—a sign, perhaps, of a field of investigation worthy of further cultivation. In the introduction to this paper the importance of hypotheses in the advancement of medical science was explained, with the suggestion that a sign of merit was current usefulness rather than a pretence of final truth. With this justification an outline may be given of some working hypotheses designed to stimulate experiments on sensitization.

The asthma–urticaria type of reaction is evoked in certain tissues by the combination of a specific antibody, which is derived from the patient's plasma globulin, with appropriate antigens. These antigens are proteins encountered in the natural environment, are of medium molecular size, are usually relatively stable to drying, and have presumably induced sensitization on some previous occasions when inhaled or ingested by the patient. The reactions in various tissues responsible for the symptoms and signs are mediated by the release of pharmacologically active substances, among which a base having histamine-like properties is prominent; subsequent neutralization of reaction products may be carried out by eosinophil leucocytes. Parenteral administration of the same antigen (though usually in amounts differing considerably from those absorbed under natural circumstances) can give rise to the formation of neutralizing antibodies which may reduce the degree of reaction to subsequent exposure.

Tuberculin–trichophytin type sensitization follows phagocytosis of certain forms of poorly soluble material—for example, wax—along with specific proteins derived from various micro-organisms. These phagocytes and similar wandering cells may then carry sensitivity widely through the body. On subsequent contact with specific protein—for example, tuberculin—these mononuclear cells react by releasing substances capable of dilating small blood vessels and attracting other mononuclear cells to the vicinity. Enzyme liberation may also occur, perhaps tending to digest the foreign protein and even, in sufficient concentrations, to affect also the local tissues and ground-substance. The functional activity of these mononuclear cells is controlled by circulating hormones—for example, cortisone and thyroxine.

Caution would have dictated the use of "perhaps" many times in these two paragraphs. The techniques, however, for proof or disproof are ready to hand, and hypotheses should not expect a long life. Heparinized blood can be separated by red-cell aggregation with dextran or fibrinogen; the supernatant, rich in white

cells, can be poured through glass wool, to which the polymorphs adhere. The filtrate has only to be lightly centrifuged to obtain lymphocytes—alive if suitably handled. Do these cells carry the essential properties required by the hypotheses? If so, under what circumstances? Similarly, many more experiments need to be performed before the explanation of the various types of "antibody" found in asthma can be regarded as "being on a scientific basis."

Summary

Protein sensitization in man is a suitable subject for scientific study, especially when reinforced by animal experiments. Two main types—the asthma–urticaria and the tuberculin–trichophytin type—are considered and contrasted. Some of the methods of controlling sensitization reactions are discussed. Tentative hypotheses suggesting further experimental work are outlined.

REFERENCES

Biggart, J. H. (1932). *J. Path. Bact.*, **35**, 799.
Blackley, C. H. (1873). *Experimental Researches on the Causes and Nature of Catarrhus Aestivus (Hay-fever or Hay-asthma).* London.
Bovet, D., and Staub, A. M. (1937). *C.R. Soc. Biol., Paris*, **124**, 547.
Burnet, F. M., and Fenner, F. (1949). *The Production of Antibodies*, 2nd ed. Melbourne.
Chase, M. W. (1945). *Proc. Soc. exp. Biol., N.Y.*, **59**, 134.
Code, C. F. (1937). *J. Physiol.*, **90**, 485.
Cooke, R. A., and Sherman, W. B. (1950). In *Pathologic Physiology*, edited by W. A. Sodeman, p. 706. London.
Coulson, E. J., and Stevens, H. (1949). *J. Immunol.*, **61**, 119.
Cruickshank, C. N. D. (1951). *Nature, Lond.*, **168**, 206.
d'Abreu, A. L. (1940). *Lancet*, **2**, 421.
Discombe, G. (1946). Ibid., **1**, 195.
Ebert, R. H., Sanders, A. G., and Florey, H. W. (1940). *Brit. J. exp. Path.*, **21**, 212.
Favour, C. B., Fremont-Smith, P., and Miller, J. M. (1949). *Amer. Rev. Tuberc.*, **60**, 212.
Gaddum, J. H. (1948). *British Medical Journal*, **1**, 867.
Halpern, B. N. (1950). *Acta allerg., Kbh.*, **3**, Suppl. 1, 164.
Hare, R. (1926). *Heart*, **13**, 227.
Harley, D. (1937). *Brit. J. exp Path.*, **18**, 469.
—— (1942). *Studies in Hay-fever and Asthma.* London.
Kabat, E. A. (1947). *Amer. J. Med.*, **3**, 535.
Koch, R. (1890). Quoted by Rich (1944).
Lawrence, H. S. (1949). *Proc. Soc. exp. Biol., N.Y.*, **71**, 516.
Lewis, T. (1927). *The Blood Vessels of the Human Skin and Their Responses.* London.
—— and Grant, R. T. (1926). *Heart*, **13**, 219.
Long, D. A., and Miles, A. A. (1950). *Lancet*, **1**, 492.
Loveless, M. H. (1940). *J. Immunol.*, **38**, 25.
—— (1941). Ibid., **41**, 15.
Miller, J. M., and Favour, C. B. (1951). *J. exp. Med.*, **93**, 1.
Raffel, S. (1948). *J. infect. Dis.*, **82**, 267.
Ramirez, M. A. (1919). *J. Amer. med. Ass.*, **73**, 984.
Ratner, B. (1939). *Amer. J. Dis. Child.*, **58**, 699.
Rich, A. R. (1944). *The Pathogenesis of Tuberculosis.* Springfield, Illinois.
—— and Lewis, M. R. (1932). *Bull. Johns Hopk. Hosp.*, **50**, 115.
Rimington, C., Stillwell, D. E., and Maunsell, K. (1947). *Brit. J. exp. Path.*, **28**, 309.
Salter, H. Hyde (1860). *On Asthma: Its Pathology and Treatment.* London.
Seibert, F. B. (1944). *Chem. Rev.*, **34**, 107.
Squire, J. R. (1950). *Clin. Sci.*, **9**, 127.
Stull, A., Cooke, R. A., and Chobot, R. (1931). *J. biol. Chem.*, **92**, 569.
Wadley, F. M. (1949) *Amer. Rev. Tuberc.*, **60**, 131.

The annual report of the honorary secretary of the Joint Tuberculosis Council briefly records the work of the council during the year. Probably the most important achievement was the completion and publication of forms of record for use in chest clinics. At the request of the Ministry of Health the council drew up a memorandum on the internal administration of hospitals, and members of the council also assisted the Ministry in drawing up a report on skiagraphic terminology and radiographic technique. A trial of a four-digit classification of tuberculosis was undertaken at the request of the World Health Organization.

DENTAL DISEASE AMONG 14-YEAR-OLD LONDON SCHOOL-CHILDREN IN 1947 AND 1950

BY

MAY MELLANBY

AND

HELEN MELLANBY, M.D., Ph.D.

with the assistance of

JOAN JOYNER, B.Sc., and MARION KELLEY

(From the Nutrition Building, National Institute for Medical Research, Mill Hill, London)

The Education Act of 1944, which raised the school-leaving age to 15, gave the opportunity for making dental surveys of the 14-year-old group. This age is suitable for the examination of the permanent teeth, as most types have erupted, with the exception of the third molars, while few deciduous teeth remain to be shed. It also provides an overall picture of the state of dental fitness of a section of children the majority of whom are about to leave school, and as such it will no doubt be of interest to the public health authorities.

The two surveys with which this paper is concerned were carried out during the winter months of 1947–8 and 1950–1, but for the sake of brevity they will be referred to as the 1947 and 1950 surveys. The London County Council very kindly afforded facilities for making the inspections, all of which took place in schools under their authority, the number of children examined being 1,216 in the earlier year and 1,089 in the later. These children were unselected samples distributed between modern, technical, and grammar secondary schools, the proportions from each bearing a rough relation to that of the total child population attending the different kinds of secondary schools in the area. In both surveys approximately 72% were from the modern schools, 12% from technical schools, and 16% from grammar schools. Since more children attend modern schools, any differences between the teeth of these children in the two surveys have more influence on the total figures than have the differences between the teeth of technical or grammar pupils. The samples of children from the latter kinds of school were too small to give more than an indication of possible differences between them and the moderns, especially where individual types of teeth are concerned.

The examination procedure and the charts used for recording the dental condition of the children were basically the same as those employed in the surveys of 5-year-olds from 1943 onwards (see Mellanby and Coumoulos, 1946), but certain adaptations were made to suit the charts for use with the permanent dentition (see Chart). Although external structure (as gauged by M. Mellanby's probe method), the incidence and extent of caries, mottling of the enamel, tartar, gingivitis, alignment, and occlusion were recorded, in the present paper only the results relating to the incidence and extent of caries, gingivitis, and tartar are given.

Methods

Each child's mouth was carefully examined by one of us with a standard probe and illuminated mirror, the results for each individual being separately charted.

PERMANENT TEETH

Name _____ Date of Birth _____ No. _____

School _____ Date _____

Gingivitis 0, 1, 2, 3														
Tartar														
Mottling 0, 1, 2, 3														
M-hypoplasia (0, 1, 2, 3) & G														
Caries 0, 1, 2, 3														
Teeth Present	7	6	5	4	3	2	1	1	2	3	4	5	6	7
Teeth Present	7	6	5	4	3	2	1	1	2	3	4	5	6	7
Caries 0, 1, 2, 3														
M-hypoplasia (0, 1, 2, 3) & G														
Mottling 0, 1, 2, 3														
Tartar														
Gingivitis 0, 1, 2, 3														

State of mouth _____

Alignment _____

Occlusion _____

Stain _____

The expression of the incidence of caries alone, whether given as a percentage or as the D.M.F. (decayed, missing, filled) figure, does not in our opinion provide a complete picture of the state of the teeth, as a group of individuals with small cavities would appear on paper to have the same amount of caries as a group in which the cavities were large. In these surveys, therefore, when caries was considered to be present in a tooth an attempt was made to assess the extent by grading the lesion 1, 2, or 3 according to the following criteria :

Grade C_1. Slight Caries.—(*a*) Pits and fissures suspected of caries on account of the probe sticking. (*b*) Indefinite approximal caries (i.e., presence strongly suspected). (*c*) Tiny visible cavities up to about 1 mm. in diameter.

Grade C_2. Moderate Caries.—Cavities larger than those in grade 1, but not involving more than one-quarter of the crown.

Grade C_3. Severe Caries.—Cavities involving more than one-quarter of the crown. In this last category were also placed all teeth assumed to have been extracted for caries, and those of which only carious roots remained.

When a history was obtained of teeth extracted for regulation or following trauma, these were excluded from all the results. Filled teeth were counted as having been decayed, since it is unlikely that any of the children examined would have had " preventive " fillings inserted. In assessing the probable size of a cavity before treatment a small allowance was made for removal of extra tooth substance in preparation. For instance, very small amalgam fillings in fissures of the molar teeth were graded C_1, and fillings anywhere which only just exceeded one-quarter of the crown were graded C_2. From this assessment of caries extent, an average caries figure (A.C.F.) was derived according to the formula set out in the footnote to Table IV. It is fully realized that this method of assessing the extent of caries can give only an approximate result, as it relies largely on naked-eye inspection, but when it is employed by the same investigators for successive surveys it gives comparable results.

A small proportion of teeth (approximately 3%), chiefly upper canines, upper and lower premolars, and second molars, remained unerupted. Each case of apparent non-eruption was judged on its merits; for instance, when the deciduous precursor was either *in situ* or had very recently been shed, or the outline of the permanent tooth could be seen through the gum, it was then obvious that a given tooth had not erupted. In the case of the second molars the decision of non-eruption *versus* extraction was sometimes more difficult, but the appearance of the gum combined with the stage of eruption of other teeth, especially the other second molars in the same mouth, usually provided sufficient evidence one way or another.

When no caries was detected in any of a child's permanent teeth, and there was also no evidence of any such teeth having been extracted or filled on account of decay, that child was considered for the purpose of this investigation to be caries-free, though no doubt it might have been found to have decay had ancillary aids over and above a probe and mirror been used. If only a small amount of caries was detected in a child, such as one, two or three grade 1 cavities, and there had again been no extractions or fillings, that child was placed in a separate category labelled " slight caries " to distinguish it from children with more extensive lesions. These two groups, the " caries-free " and those with " slight caries," together give an idea of the proportion of children who at 14 would be considered to have " good " mouths.

Gingivitis, when present, was roughly divided into three grades, depending on the degree of swelling and hyperaemia, especially of the interdental papillae, coupled with the extent of this in each mouth. Children with " normal " gingivae were classified as 0. Their gum tissue was a uniform pale pink with thin edges closely adherent to the tooth surfaces, the spaces between adjoining teeth being filled by the points of the interdental papillae. The appearance of the gum surface was matt, due to the presence of stippling (King, 1945) as opposed to the shiny surface seen in abnormal tissues. Grade 1 (mild gingivitis) included children with shiny and slightly swollen papillae between a few teeth, as was most commonly found in the lower incisor region. Grade 2 (moderate gingivitis) contained those children in whom large areas of the gingivae were slightly affected, or who had considerable amounts of swelling and hyperaemia round a few teeth, with the rest little affected. Grade 3 (severe gingivitis) was used for those children with very obviously thickened, reddened, and swollen gum tissue. In some individuals this might be confined to the anterior teeth, but in others it was more extensive. A few in this group had advanced gingival disease with ulceration and pocketing.

Tartar deposits on individual teeth were graded on the charts as 1, 2, or 3, according to whether they covered up to one-third, two-thirds, or the whole of the buccal or lingual surface. From these figures an average assessment for each mouth was obtained, and the children were then graded into four categories—0, 1, 2, and 3.

Caries

The number of children examined in the two surveys and distributed between the three kinds of secondary school are given in Table I, column 2. The totals for 1950 were rather fewer, but the proportions attending the modern, technical, and grammar schools were the same on each occasion. In the 1947 survey 54% of the children were boys and 46% were girls, whereas in 1950 the respective percentages were 55.8 and 44.2, the average age on both occasions being 14 years 5 months.

TABLE I.—*Children Caries-free or with Slight Caries and the Average Number of Carious Permanent Teeth per Child (D.M.F.)*

1	2		3		4		5	
Variety of Secondary School	No. of Children Examined		Percentage Caries-free*		Percentage with Slight Caries* (Three or Less C_1 Cavities)		Average No. of Carious Teeth per Child (D.M.F.)	
	1947	1950	1947	1950	1947	1950	1947	1950
Modern ..	878	784	11·3	17·0	11·2	17·9	3·99	3·65
Technical ..	151	136	13·2	14·0	16·6	15·4	3·68	4·04
Grammar ..	187	169	11·2	13·6	19·3	11·8	3·90	4·20
Total ..	1,216	1,089	11·5	16·1	13·1	16·8	3·94	3·79

* See text for definitions.

The proportion of *children* considered to be caries-free, according to the standards used, increased from 11.5% in 1947 to 16.1% in 1950 (Table I, column 3). This increase was spread over the three kinds of school, being more pronounced in the modern than in the others. The total percentage of children with very little decay (Table I, column 4) also increased, but this was entirely because the considerable improvement in the modern pupils more than compensated for the reduced number of such children in technical and grammar schools. The average number of carious teeth per child (equivalent to the D.M.F. per child of some authors) showed a slight overall reduction, which was again achieved by the modern schools' improvement exceeding the somewhat worsened state of affairs in the others. More boys than girls were found to be caries-free in 1950—about 19% as compared with 12%—whereas in 1947 the difference in this respect was negligible.

In Table II an attempt has been made to gather together from the literature a few comparative caries figures for other groups, mostly children of fairly similar age who had also been examined with a probe and mirror. From this table it will be seen that in some communities, such as Hagerstown (U.S.A.) and Newfoundland, caries incidence was high, only 4.6 and 0.8% respectively of the children examined being caries-free at 14 years of age. Children from Chicago, Trinidad, and American Indian reserves gave intermediate figures of 14.4, 13.8, and 23% respectively of individuals caries-free. Where caries incidence in this age group was considered to be comparatively low, as in the Isle of Lewis, Scotland, the town of South Shields, England, and Northern Italy, the percentages of caries-free children were 30.8, 25.8–50.6, and 38.4 respectively. African and, more recently, Indian children were found by M. Mellanby to be remarkably free from caries; in the latter case 65.8% of the 14-year age group at Lucknow were in this category. From these figures it will be realized that the London children in 1950, with 16.1% of individuals free from decay, were better than some groups, though a long way from the best so far reported, even for this country—for example, Lewis and South Shields.

The percentage of teeth present in the London children at the time of inspection are given in Table III. These figures represent the teeth actually seen in the mouth (extractions as well as unerupted teeth being omitted here), as compared with the possible total if every child had 28 permanent teeth erupted. The very few third molars observed were excluded. The majority of the 28 teeth per child were *in situ*, the percentages being 94.8 in 1947 and 95.9 in 1950.

Individual differences in the proportion of the various types of teeth present in pupils from the three kinds of school were on the whole very small. In 1947 the percentages of upper and lower first molars were highest in the grammar schools and lowest in the modern, the difference being between 6 and 7%. In 1950 there was no difference between the schools as regards upper first molars, but of the lower first molars the grammar schools now had the lowest percentage and the technical the highest, the discrepancy between them being 6.8%.

TABLE II.—*Comparative Figures for Dental Caries in Different Parts of the World*

Place	Author	Date of Survey	No. of Individuals Examined	Age Group	Percentage of Individuals Caries-free	Percentage of Teeth Carious or D.M.F. per 100 Teeth	Average No. of Decayed Teeth per Person (D.M.F.)	Comments
Africa, Kenya ..	M. Mellanby (1934)	1929	103	Young adults	84	2·01 (approx.)	0·56 (approx.)	
Africa, Zanzibar ..	M. Mellanby (1934)	1929	154	Aver. 27 years	50		1·5	Deciduous and permanent teeth
U.S.A. American Indians in reserves..	Klein and Palmer (1937)	1929–33	1,300	5–16 ,,	23	11·1 (approx.)	3·12	Indians distributed between 76 reserves in 16 States
Scotland, Isle of Lewis	King (1940)	1937	185	14 and 15 ,,	30·8	8·5	2·2	Rural fishing communities
U.S.A., Hagerstown, Madison	Klein *et al.* (1938)	1937	364	13–15 ,,	4·6	19·2	5·2	Described as typical East U.S.A. small town
U.S.A., Chicago ..	Dean *et al.* (1941)	1939	2,832	14 ,,	14·4 (average)	—	4·73 (average)	Average of eight separate communities
Italy (four northern cities)	Schour and Massler (1947)	1945	475	12–14 ,,	53·4	—	1·05	Deciduous and permanent teeth
		1945	247	11–15 ,,	38·4	—	2·02	Permanent teeth
Trinidad	King and Martin (1951)	1948	406	16–20 ,,	13·8	21·7	5·37	East Indian and Negro children
British Guiana ..			100	12–14 ,,	13·0	18·4	4·91	
Newfoundland ..	H. Mellanby (unpublished work)	1948	595	12–14 ,,	0·8	30·7	8·39	
England, South Shields	Weaver (1950)	1943	500	14 ,,	25·8	—	2·4	1·4 p.p.m. fluorine in water supply
		1949	500	12 ,,	50·6	—	1·3	
England, North Shields	Weaver (1950)	1943	500	12 ,,	4·8	—	4·3	Negligible fluorine
		1949	500	12 ,,	26·4	—	2·4	
India, Lucknow ..	M. Mellanby (unpublished work)	1951	266	12 ,,	65·8	2·71		
		1951	801	13–20 ,,	60·8	3·4	0·95	

A proportion of the spaces for unerupted permanent teeth were still occupied by deciduous predecessors; for example, in 1950 there were 139 deciduous teeth still retained, of which 33.1% were upper canines and 57.6% were second molars. No records were made of decay in these teeth, all the figures for caries incidence and extent given in this paper referring to the permanent dentition only.

TABLE III.—*Percentage of Permanent Teeth of Each Type In Situ*

Type of Tooth	Variety of School	1947		1950	
Upper jaw:					
Central incisors ..	Modern	99·0	99·2	98·9	98·8
	Technical	99·7		99·6	
	Grammar	99·7		99·1	
Lateral incisors ..	Modern	97·8	98·2	98·3	98·2
	Technical	98·7		98·5	
	Grammar	99·5		97·9	
Canines	Modern	97·3	97·7	97·4	96·7
	Technical	98·0		96·0	
	Grammar	98·9		94·4	
1st premolars ..	Modern	97·8	97·5	99·1	98·6
	Technical	96·7		98·5	
	Grammar	96·8		97·6	
2nd premolars ..	Modern	91·6	91·9	92·8	93·3
	Technical	91·1		93·8	
	Grammar	94·1		95·3	
1st molars	Modern	90·5	92·1	93·6	93·6
	Technical	95·7		93·8	
	Grammar	96·8		93·8	
2nd molars ..	Modern	93·8	93·3	96·8	96·4
	Technical	90·2		95·6	
	Grammar	93·5		95·9	
Lower jaw:					
Central incisors ..	Modern	99·8	99·9	99·7	99·6
	Technical	100		99·3	
	Grammar	100		99·4	
Lateral incisors ..	Modern	99·7	99·8	99·7	99·7
	Technical	100		99·6	
	Grammar	100		99·4	
Canines	Modern	99·4	99·5	99·7	99·8
	Technical	99·7		99·6	
	Grammar	100		100	
1st premolars ..	Modern	95·7	95·4	97·4	97·5
	Technical	93·4		97·4	
	Grammar	95·7		99·1	
2nd premolars ..	Modern	83·2	84·2	87·0	87·6
	Technical	84·4		89·0	
	Grammar	88·5		89·9	
1st molars	Modern	83·2	85·1	87·6	87·0
	Technical	89·1		89·0	
	Grammar	90·9		82·2	
2nd molars	Modern	93·7	93·4	96·7	95·8
	Technical	92·4		96·3	
	Grammar	92·5		95·6	
Totals for upper and lower jaws	Modern	94·5	94·8	95·9	95·9
	Technical	94·9		96·1	
	Grammar	96·2		95·7	

A proportion of the spaces for unerupted permanent teeth were still occupied by deciduous predecessors; for example, in 1950 there were 139 deciduous teeth still retained, of which 33.1% were upper canines and 57.6% were second molars. No records were made of decay in these teeth, all the figures for caries incidence and extent given in this paper referring to the permanent dentition only.

An analysis of the caries results for both surveys and for each type of permanent tooth in the combined schools is given in Table IV. Column 2, compiled from the numbers of teeth inspected plus those extracted for caries, shows the total numbers on which the analysis is based. As is usual in most civilized communities, the tooth most frequently attacked by disease was the lower first molar (over 60% in each survey being carious), with the upper first molar coming next. The least attacked were the canines, the lower incisors, and the lower first premolars.

The caries incidence for all types of teeth together was 14.6% in 1947 and 13.9% in 1950 (Table IV, column 7). When the different types of teeth are considered individually, however, it will be seen that there was more caries in 1950 among the upper incisors and rather less in the first molars. The A.C.F. for these teeth (column 8) showed corresponding increases in the upper incisors and decreases in the first molars. The very slight overall improvement in the caries position in 1950 compared with 1947, therefore, was not achieved by a uniform reduction of decay, but rather by the reduction in the incidence of first molar decay exceeding the increase experienced in the upper incisors.

The caries incidence and extent in the three varieties of school are set out in Table V. From the total percentages at the bottom of column 7 it will be seen that in 1947 the technical schools had the lowest overall caries incidence and the modern schools the highest, though the difference between them was very small (13.7% compared with 14.8% of teeth affected). By 1950 there had been a slight reduction of caries in the modern schools (from 14.8 to 13.4%), whereas in the other two groups the incidence had apparently increased a little (from 13.7 to 14.8% in the technical schools and from 14.5 to 15.4% in the grammar schools), though as the samples were small too much importance should not be attached to individual results for technical and grammar schools. It will also be seen from Table V, column 7, that the improvement in the caries position

TABLE IV.—*Caries Incidence and Extent in the Combined Schools*

1	2		3		4		5		6		7		8	
Type of Tooth	Total No. of Teeth (including Extractions)		Teeth Graded C_0 (No Caries)		Teeth Graded C_1 (Slight Caries)		Teeth Graded C_2 (Moderate Caries)		Teeth Graded C_3 (Severe Caries)		Total Carious Teeth (Equiv. of D.M.F. per 100 Teeth)		A.C.F.*	
	1947	1950	1947	1950	1947	1950	1947	1950	1947	1950	1947	1950	1947	1950
Upper jaw:			%	%	%	%	%	%	%	%	%	%		
Central incisors ..	2,415	2,159	93·9	90·6	3·1	4·4	2·5	4·1	0·5	0·9	6·1	9·4	0·10	0·15
Lateral ,, ..	2,392	2,141	95·0	93·2	2·3	3·6	2·3	2·9	0·4	0·4	5·0	6·8	0·08	0·10
Canines	2,380	2,107	99·4	99·9	0·3	0·1	0·2	0·1	0·2	—	0·6	0·2	0·01	0·002
1st premolars ..	2,379	2,152	95·1	95·0	1·8	2·4	2·6	2·0	0·5	0·6	4·9	5·0	0·09	0·08
2nd ,, ...	2,237	2,035	92·9	94·3	3·3	2·8	3·0	2·2	0·8	0·6	7·1	5·7	0·12	0·09
1st molars	2,427	2,178	44·7	50·3	20·0	20·3	23·5	19·9	11·8	9·5	55·3	49·7	1·02	0·89
2nd ,, ...	2,270	2,105	82·5	84·6	13·6	10·5	3·6	4·2	0·4	0·7	17·5	15·4	0·22	0·21
Total for upper jaw ..	16,500	14,877	86·1	86·7	6·3	6·4	5·5	5·1	2·1	1·8	13·9	13·3	0·24	0·22
Lower jaw:														
Central incisors ..	2,429	2,170	99·1	99·5	0·5	0·3	0·4	0·1	0·04	—	0·9	0·5	0·01	0·01
Lateral ,, ..	2,427	2,171	99·3	99·8	0·3	0·0	0·4	0·1	0·04	—	0·7	0·2	0·01	0·003
Canines	2,420	2,173	99·9	100·0	0·1	—	—	0·05	—	—	0·1	0·05	0·001	0·001
1st premolars ..	2,323	2,128	99·1	99·1	0·2	0·1	0·4	0·4	0·3	0·4	0·9	0·9	0·02	0·02
2nd ,, ...	2,055	1,910	96·1	96·9	1·3	1·1	2·0	1·4	0·6	0·7	3·9	3·1	0·07	0·06
1st molars	2,431	2,177	33·6	38·5	16·4	18·5	28·3	25·0	21·7	18·0	66·4	61·5	1·38	1·22
2nd ,, ...	2,279	2,107	67·6	66·4	20·0	20·2	10·7	10·6	1·7	2·8	32·4	33·6	0·46	0·50
Total for lower jaw ..	16,364	14,836	84·7	85·6	5·5	5·8	6·1	5·5	3·6	3·2	15·3	14·4	0·29	0·28
Total for u. and l. jaws	32,864	29,713	85·4	86·1	5·9	6·1	5·8	5·3	2·9	2·5	14·6	13·9	0·26	0·24

* A.C.F. (average caries figure) = $\frac{\text{Total caries figure}}{\text{Total number of teeth, including extractions}} = \frac{\text{No. of } C_1 + 2(\text{No. of } C_2) + 3(\text{No. of } C_3)}{\text{Total number of teeth, including extractions}}$

of the modern schools in 1950 was largely attributable to the marked reduction in the caries incidence in the first molars, whereas in the other varieties of school there was an increased incidence in these teeth. The upper incisors showed more decay in all three kinds of school in 1950, but it was greater in the technical and grammar than in the modern schools. These differences are also seen in the average caries figures (column 8). The greatest discrepancies between the schools in the respective surveys occurred in the lower second molars in 1947 and in the upper and lower first molars in 1950.

When the percentage of carious teeth found in the London children in 1947 and 1950—namely, 14.6 and 13.9—are compared with the findings in other groups in various parts of the world (see Table II), it will be seen that the London children occupy an intermediate position. They have less decay than West Indian, Newfoundland, and some U.S.A. children, but more than children from Lewis (Scotland), and many more than groups of Africans and Indians.

Table VI, which indicates the amount of dental treatment given to the London children, shows that approximately the same percentage of carious teeth had been extracted in the case of the children examined in the two surveys—12.3 in 1947 and 11.5 in 1950—while there was a slight falling-off in the percentage of carious

TABLE V.—*Caries Incidence and Extent in Three Varieties of School*

1	2	3		4		5		6		7		8	
Type of Tooth	School	Teeth Graded C_0 (No Caries)		Teeth Graded C_1 (Slight Caries)		Teeth Graded C_2 (Moderate Caries)		Teeth Graded C_3 (Severe Caries)		Total Carious Teeth (Equiv. of D.M.F. per 100 Teeth)		A.C.F.*	
		1947	1950	1947	1950	1947	1950	1947	1950	1947	1950	1947	1950
Upper jaw:		%	%	%	%	%	%	%	%	%	%		
Central incisors	Modern	94·0	91·7	3·0	4·5	2·4	2·9	0·6	0·8	6·0	8·2	0·10	0·13
	Technical	93·1	86·7	3·3	5·9	3·0	7·0	0·6	0·4	6·9	13·3	0·11	0·21
	Grammar	94·4	88·1	2·9	3·0	2·4	7·4	0·3	1·5	5·6	11·9	0·09	0·22
Lateral incisors	Modern	95·3	94·2	2·3	4·0	2·0	2·2	0·4	0·3	4·7	5·8	0·08	0·09
	Technical	92·6	91·8	3·3	5·6	3·7	2·2	0·3	0·4	7·4	8·2	0·12	0·11
	Grammar	95·4	90·0	1·6	3·6	2·7	5·4	0·3	0·9	4·6	10·0	0·08	0·17
Canines ..	Modern	99·3	99·8	0·2	0·1	0·2	0·1	0·3	—	0·7	0·2	0·01	0·003
	Technical	99·0	100·0	0·7	—	0·3	—	—	—	1·0	—	0·01	—
	Grammar	100·0	100·0	—	—	—	—	—	—	—	—	—	—
1st premolars ..	Modern	94·9	95·2	2·0	2·4	2·7	1·7	0·5	0·6	5·1	4·8	0·09	0·08
	Technical	95·2	93·7	1·0	2·2	3·1	3·7	0·7	0·4	4·8	6·3	0·09	0·11
	Grammar	95·9	95·5	2·0	2·1	1·6	2·1	0·5	0·3	4·1	4·5	0·07	0·07
2nd premolars..	Modern	92·9	94·2	3·5	2·7	2·7	2·6	0·9	0·5	7·1	5·8	0·12	0·09
	Technical	94·9	94·9	1·8	2·7	2·9	1·2	0·4	1·2	5·1	5·1	0·09	0·09
	Grammar	91·5	94·8	3·4	3·1	4·5	1·2	0·6	0·9	8·5	5·2	0·14	0·08
1st molars ..	Modern	45·4	54·5	18·5	19·0	22·6	17·0	13·5	9·6	54·6	45·5	1·04	0·82
	Technical	41·7	40·1	23·9	27·6	26·5	23·5	7·9	8·8	58·3	59·9	1·01	1·01
	Grammar	43·8	39·1	23·8	20·4	25·7	30·8	6·7	9·8	56·2	60·9	0·95	1·11
2nd molars ..	Modern	81·6	84·3	14·1	11·2	3·9	4·0	0·4	0·6	18·4	15·7	0·23	0·21
	Technical	87·2	86·2	9·6	9·2	2·6	3·8	0·7	0·8	12·9	13·8	0·17	0·19
	Grammar	82·9	85·0	14·3	8·3	2·9	5·8	—	0·9	17·2	15·0	0·20	0·23
Lower jaw:													
Central incisors	Modern	99·0	99·7	0·5	0·1	0·5	0·1	0·1	—	1·0	0·3	0·02	0·004
	Technical	100·0	99·6	—	0·4	—	—	—	—	—	0·4	—	0·004
	Grammar	98·4	98·5	1·1	1·2	0·5	0·3	—	—	1·6	1·5	0·02	0·02
Lateral incisors	Modern	99·1	99·9	0·3	—	0·5	0·1	0·1	—	0·9	0·1	0·01	0·003
	Technical	100·0	99·6	—	—	—	0·4	—	—	—	0·4	—	0·007
	Grammar	99·5	99·7	0·5	0·3	—	—	—	—	0·5	0·3	0·01	0·003
Canines ..	Modern	99·8	99·9	0·2	—	—	0·1	—	—	0·2	0·1	0·002	0·001
	Technical	100·0	100·0	—	—	—	—	—	—	—	—	—	—
	Grammar	100·0	100·0	—	—	—	—	—	—	—	—	—	—
1st premolars ..	Modern	99·0	99·0	0·2	0·1	0·5	0·3	0·3	0·5	1·0	1·0	0·02	0·02
	Technical	98·6	99·6	0·4	—	0·7	0·4	0·4	—	1·4	0·4	0·03	0·008
	Grammar	100·0	98·8	—	0·3	—	0·6	—	0·3	—	1·2	—	0·02
2nd premolars..	Modern	95·9	96·7	1·3	1·0	2·2	1·4	0·6	0·7	4·1	3·1	0·07	0·06
	Technical	96·9	96·3	1·2	1·7	1·6	1·2	0·4	0·8	3·1	3·7	0·05	0·07
	Grammar	96·4	97·4	1·2	1·0	1·5	1·6	0·9	—	3·6	2·6	0·07	0·04
1st molars ..	Modern	32·5	40·6	15·6	19·1	27·1	22·3	24·8	18·0	67·5	59·4	1·44	1·16
	Technical	37·4	38·0	17·2	15·8	29·5	33·5	15·9	14·7	62·6	64·0	1·24	1·27
	Grammar	35·8	30·9	19·5	18·1	32·9	30·9	11·8	20·2	64·2	69·1	1·21	1·40
2nd molars ..	Modern	67·1	64·8	19·6	22·3	11·2	9·8	2·1	3·0	32·9	35·2	0·48	0·51
	Technical	74·9	70·9	16·9	16·6	7·9	9·8	0·4	2·6	25·1	29·1	0·34	0·44
	Grammar	64·2	69·6	24·6	13·5	10·1	15·0	1·2	1·8	35·8	30·4	0·50	0·49
All types	Modern	85·2	86·6	5·8	6·2	5·7	4·7	3·3	2·5	14·8	13·4	0·27	0·23
	Technical	86·3	85·2	5·7	6·3	6·0	6·3	2·0	2·2	13·7	14·8	0·24	0·25
	Grammar	85·5	84·6	6·7	5·4	6·1	7·3	1·6	2·7	14·5	15·4	0·24	0·25

* See footnote to Table IV.

TABLE VI.—*Treatment and Arrest of Decay*

1	2		3						4		5	
Variety of Secondary School	No. of Carious Teeth		Treatment of Carious Teeth: Percentage Extracted		Percentage Filled		Total Percentage Treated		Percentage of Total Carious Teeth with Moderate and Severe Caries Untreated ($C_2 + C_3$)		Percentage of *Untreated* Carious Teeth Showing Arrest of Decay	
	1947	1950	1947	1950	1947	1950	1947	1950	1947	1950	1947	1950
Modern ..	3,500	2,862	13·9	11·6	41·1	33·3	55·0	44·9	17·8	21·9	3·68	2·86
Technical ..	556	550	9·2	9·3	45·5	52·9	54·7	62·2	17·8	14·5	3·17	2·88
Grammar ..	737	710	7·1	12·8	54·4	52·8	61·5	65·5	8·8	12·5	4·23	1·22
Total ..	4,793	4,122	12·3	11·5	43·6	39·3	55·9	50·8	16·4	19·3	3·69	2·88

TABLE VII.—*Comparative Gingivitis Figures for Older Children*

Place	Author	Date of Survey	No. of Children Examined	Age Group	Percentage of Children Free from Gingivitis	Percentage of Children with Mild Gingivitis	Percentage of Children with Moderate Gingivitis	Percentage of Children with Severe Gingivitis	Average Gingivitis Figure
London	Mellanby and Mellanby	1947	1,192*	14 years	26·3	30·5	33·8	9·3	1·26
		1950	1,069*	14 ,,	14·9	39·0	39·1	7·0	1·38
Scotland, Isle of Lewis (rural)	King (1940)	1937	185	13–15 ,,	3·8	—	—	—	1·11
Newfoundland ..	H. Mellanby (unpublished)	1948	595	14 ,,	21·0	28·7	36·6	13·6	1·43
Trinidad	King and Martin (1951)	1948	406	12–14 ,,	17·0	—	—	—	0·95
British Guiana ..			100	12–14 ,,	11·0	—	—	—	1·30
India, Lucknow ..	M. Mellanby (unpublished)	1951	265	14 ,,	27·2	43·8	23·0	6·0	1·08
			472	15–20 ,,	28·8	39·2	25·0	7·0	1·10

* In a few instances gingivitis and tartar figures on the charts were found to be incomplete; these charts were therefore excluded in preparing Tables VII and VIII.

teeth which had been filled—43.6 in 1947 compared with 39.3 in 1950. There was therefore an overall reduction of 5% in the proportion of carious teeth treated as between the 1947 and 1950 surveys. A comparison of the figures for the three kinds of school shows that technical and grammar schools had had some increase in treatment. It was in the modern schools where this had been reduced, but it will be noted that it was the children in these same schools who showed a reduction in caries incidence (see Table V). A small amount of apparently "arrested" caries was found in the two surveys. This occurred in 3.69% of all untreated carious teeth in 1947 and 2.66% in 1950 (see Table VI, column 5).

Gingivitis and Tartar

The results of the gingivitis estimations based on the criteria described above are given in Table VII. Here it will be seen that only 26.3% of the children in 1947 and 14.9% in 1950 were considered to have no gingivitis, approximately two-thirds in both years had a slight or moderate degree, while relatively few, 9.3 and 7% respectively, were counted as having a severe type. It would therefore appear that gingivitis was a common condition among these children, and that its incidence had apparently increased between 1947 and 1950.

A few comparative figures for other surveys are also given in Table VII, showing that gingivitis, at least in a mild form, is widespread, though its occurrence seems to have no simple explanation. It is always difficult to compare the findings for the incidence and degree of gingivitis of different workers, since the standards vary, quite apart from personal factors in the examinations. For this reason the investigations to which reference is made here are confined to those of ourselves and a former colleague, J. D. King, who has latterly made an experimental and clinical study of the subject. He employs a more detailed classification than we, so that his results for the West Indian children in Trinidad and British Guiana are not strictly comparable with our findings in London, Newfoundland, and India.

TABLE VIII.—*The Association Between Tartar Deposits and the Occurrence of Gingivitis*

1	2		3		4	
Grade of Tartar	No. of Children		Percentage of Children with Gingivitis		Average Gingivitis Figure	
	1947	1950	1947	1950	1947	1950
0	469	366	65·5	81·7	0·99	1·24
1 (slight)	364	400	71·2	85·5	1·17	1·34
2 (moderate) ..	285	259	84·9	87·3	1·59	1·54
3 (extensive) ..	74	44	94·6	97·7	2·14	2·00
	1,192	1,069	73·7	85·1	1·26	1·38

Table VIII (column 2) gives the number of London children with various grades of tartar deposition from 0 to 3 (see above), from which may be calculated the incidence of the different degrees and the average tartar figures. The same table (columns 3 and 4) also gives the associated occurrence and extent of gingivitis. The areas of the mouth most commonly affected by tartar were, as is usual, the upper first molar and the lower incisor regions. Some 5% fewer children were free from tartar in 1950 as compared with 1947, but 7% more had only a slight degree; the average tartar figures (calculated on the same basis as the average caries figures) will be found to be almost identical for the two surveys.

Although many of the children with no tartar had gingivitis, this was generally of a milder degree than that experienced by children having calculus. With increasing amounts of tartar the incidence of gingivitis was also raised, until with extensive deposits (grade 3) 94.6 and 97.7% respectively of the children in the two surveys had some degree of parodontal abnormality (Table VIII, column 3). The average gingivitis figure also increased considerably with moderate and extensive amounts of tartar (Table VIII, column 4). In the Trinidad and Jamaican children examined by King a high degree of association was found to exist between gingivitis and tartar deposition when the location of the two was restricted to the anterior part of the mandible (King and Martin, 1951).

Conclusions

On the whole we were favourably impressed by the state of these 14-year-old children's teeth. They were better than we had anticipated, especially when allowance was made for all the difficulties of the present time. Any differences between the overall caries incidence in the teeth examined in the two surveys were slight, but some shift of caries away from the first molars was discernible, and with this went an increase in the disease among other teeth, especially the upper incisors. Both surveys showed a high incidence of gingivitis, but there was appreciably more in 1950 than in 1947, and also slightly more tartar.

Summary

Two surveys of 14-year-old London County Council school-children from modern, technical, and grammar schools provide the clinical material for this paper. The inspections were made with a probe and mirror.

The proportion of children found to be free from caries, according to the standards used, was 11.5% in 1947 and 16.1% in 1950. These results are compared with figures from different parts of the world, including other areas of Britain.

A detailed analysis of the incidence and extent of caries in the different types of teeth is given for all the schools

taken together in the two surveys. A separate analysis for the three kinds of school is also given, but with few exceptions the differences between them were not large. A total of 14.6% of the teeth in 1947 were carious, whereas for 1950 the figure was 13.9%. Comparative figures for caries incidence in other groups of children are given.

Only small differences were found between the two surveys as regards the amount of caries in the different types of teeth, but in 1950 more upper incisors and fewer first molars were carious than in the first survey.

The amount of treatment (fillings and extractions) which the teeth had received is briefly considered. An overall reduction of 5% was noted in 1950 as compared with 1947.

Some degree of gingivitis was found to occur in 73.7% of the children examined in 1947 and in 85.1% of those seen in 1950. That this is a common finding in this age group is substantiated by figures for other surveys.

Tartar deposits were frequently found, and there appeared to be some relation between the amount of tartar and the incidence and extent of gingivitis.

We wish to thank the London County Council and Sir Allen Daley for permission to carry out the inspections, and we are much indebted to the head teachers and staffs of the schools for all the help they gave with the actual examinations. Our thanks are also due to Miss I. Allen, of the Medical Research Council's Statistical Department, for advice, and to the Medical Research Council for financing the work.

REFERENCES

Dean, H. T., Jay, P., Arnold, F. A., jun., and Elvove, E. (1941). *Publ. Hlth Rep., Wash.*, **56**, 761.
King, J. D. (1940). *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 241.
—— (1945). *Dent. Rec.*, **65**, 9, 32, 55.
—— and Martin, W. J. (1951). *Brit. dent. J.*, **90**, 35, 63.
Klein, H., and Palmer, C. E. (1937). *Publ. Hlth Bull., Wash.*, No. 239.
—— —— and Knutson, J. W. (1938). *Publ. Hlth Rep., Wash.*, **53**, 751.
Mellanby, M. (1934). *Spec. Rep. Ser. med. Res., Coun., Lond.*, No. 191.
—— and Coumoulos, H. (1946). *British Medical Journal*, **2**, 565.
Schour, I., and Massler, M. (1947). *J. Amer. dent. Ass.*, **35**, 1.
Weaver, R. (1950). *Brit. dent. J.*, **88**, 231.

INTESTINAL MACROCYTIC ANAEMIA

BY

G. M. WATSON, D.Ph., M.B., B.S., M.R.C.P.*

AND

L. J. WITTS, M.D., F.R.C.P.

(From the Nuffield Department of Clinical Medicine, the Radcliffe Infirmary, Oxford)

The occasional association of pernicious anaemia with intestinal stricture was discovered by Faber in 1895. In the succeeding years more cases were recorded, and in 1924 Seyderhelm and his associates claimed to have reproduced the syndrome in dogs. In 1929 Little, Zerfas, and Trusler found a blood picture typical of pernicious anaemia in a young man on whom several operations had been performed to cure an intestinal fistula which followed acute appendicitis. This appears to be the first record of pernicious anaemia in association with intestinal anastomosis as distinct from stricture. Other cases of this kind have since been reported, and the lesion has usually been either a gastro-jejuno-colic fistula or a stagnant loop of intestine. Tönnis *et al.* (1932) reported a brilliant series of experiments on culs-de-sac of the small intestine in dogs, and showed that the anaemia which sometimes developed would respond to liver extract.

*Australian National University Research Fellow.

In 1939 Barker and Hummel reviewed 51 cases of human pernicious anaemia associated with intestinal stricture or anastomosis, and we later brought the total to 60 (Cameron, Watson, and Witts, 1949a). In these 60 case reports anastomosis was the basic abnormality in 23, while in 37 one or more strictures were present. The strictures were mostly of the small intestine, but six were in the colon. Of the anastomoses 14 were entero-enterostomies or entero-colostomies, and nine were gastro-colic or high jejuno-colic fistulae.

The syndrome of gastro-colic fistula is now well known, its principle features being diarrhoea, steatorrhoea, malnutrition, and anaemia. Renshaw and his co-workers (1946) have made a careful clinical and experimental study of this condition. Dogs in which a gastro-colic fistula was made by operation developed a syndrome similar to that seen in man, including anaemia which in some cases became macrocytic and hyperchromic. In the dogs and in human cases it could be shown that there was little passage of gastric contents to the large bowel, and consequently the symptoms could not simply be due to diversion of food from the small intestine; rather were they due to contamination of the stomach and small intestine by colonic matter. In the cases of anaemia associated with stricture or anastomosis the fundamental abnormality appears to be the presence of a stagnant or obstructed portion of small intestine. All these mechanisms may lead to infection of the small intestine with colonic organisms.

Prominent Features

The salient features of pernicious anaemia in association with intestinal stenosis or anastomosis can be briefly enumerated. The tongue is often sore, but there is free acid in the gastric juice in more than half the cases. Intrinsic factor has been demonstrated in one case (Schlesinger, 1933), although it was absent in the only other case in which it was looked for (Castle *et al.*, 1931). Steatorrhoea is not necessarily present, but there have been few careful observations on the fat excretion. Subacute combined degeneration occurs in a fairly large proportion of cases. The bone marrow is megaloblastic, and the anaemia, which is macrocytic, responds to treatment with liver, though it is sometimes rather resistant. No information is available about the response to vitamin B_{12}, folic acid, or antibiotics. The anaemia may be permanently cured by surgical correction of the intestinal abnormality, though this cannot be promised with certainty. The syndrome has declined in frequency in recent years owing to the decreased incidence of intestinal tuberculosis, which has been the most frequent cause of stenosis of the small intestine, and to technical improvements in surgery, which avoid the formation of stagnant loops of intestine.

Present Investigation

The essential feature in macrocytic anaemia of intestinal origin appears to be stagnation, whether from stenosis or in a stagnant loop. The syndrome differs from Addisonian pernicious anaemia in that the secretion of hydrochloric acid and intrinsic factor by the stomach may be normal; and from sprue in that there need be no steatorrhoea. It seems particularly appropriate for experimental study because it is impossible to produce a megalocytic anaemia by operations on the stomach in animals (Cameron, Watson, and Witts, 1949b), and

pernicious anaemia does not always develop after total resection of the stomach in man (MacDonald *et al.*, 1947).

These observations led us to the working hypothesis that in pernicious anaemia the failure of gastric secretion might merely set the stage for the development of anaemia, which was actually initiated by events in the small intestine. With this idea we began a series of experiments with rats. We considered that the disadvantage of using so small an animal was outweighed by the ease with which we could make large numbers of preparations. A further point is that the diet and digestive tract resemble that of man, and we have been able to prepare extracts from rat livers which are effective in human pernicious anaemia. Adult albino rats of the Wistar strain, aged 4 to 6 months, have been used in all experiments. They have been fed on a synthetic diet (Watson, Cameron, and Witts, 1948), but anaemia will develop in animals receiving a mixed diet with plenty of animal protein (W. A. Broom, J. Emmet, and Woods, 1949, personal communication).

Experimental Technique

The initial experiments were designed to produce intestinal stricture and chronic obstruction, but although several methods were tried none was found satisfactory. The next procedure was to divide the small intestine at the junction of its upper and middle thirds and implant the lower end of the upper intestine into the side of the small intestine at the junction of the middle and lower thirds; in this way the middle third of the small intestine is by-passed. This operation is relatively easy to perform. Nearly 200 rats were prepared in this way, but only about 10% of them developed a macrocytic anaemia, and the proportion tended to lessen as the operators became more skilled. These experiments confirmed the results of other workers who had found that a large proportion of the small intestine can be removed or by-passed without anaemia resulting, and indeed the majority of the rats lived to a ripe old age. More important was the discovery that in rats which developed anaemia there was always some dilatation of the blind loop. In most cases this was limited to the proximal 6–10 cm. of the loop and the anastomotic area, but in a few there was also some dilatation of the small intestine above the anastomosis.

The Blind-loop Operation

It was therefore decided to reverse the direction of the blind loop so that now peristalsis would tend to fill instead of emptying it. This was done by dividing the small intestine at the junction of the middle and lower thirds, and anastomosing the lower portion to the side of the small intestine at the junction of its upper and middle thirds. The same segment of intestine was by-passed as in the earlier operation, but the effects were very different. The operation was technically more hazardous because peristalsis now tended to break down the anastomosis. The middle third of small intestine, aproximately 12 in. (30 cm.) long, increased in diameter and formed an easily palpable tumour. Three out of every four rats died within three weeks, but all those which survived for that time developed macrocytic anaemia.

Further experiment showed that the percentage of anaemic animals, the speed of onset of the anaemia, and the mortality of the operation were all directly proportional to the length of the loop. It was then a straightforward procedure to work out the optimum length and position of the loop. As a result of these studies all our subsequent work has been done with 3 to 4-in. (7.5 to 10-cm.) self-filling loops placed not lower than the middle of the small intestine. Culs-de-sac from the lower ileum usually fail to produce anaemia. The Table shows the overall operative and post-operative mortality of rats prepared by this final operation. It is necessary to point out that the incidence of anaemia varied considerably at different periods for no very obvious reason. Thus, in one set of experiments a yield of only a little over 10% of anaemic rats was obtained, while in another it was as high as 42%.

Operative Mortality and Incidence of Anaemia

Death within one month of operation	51·7%
Dying up to six months from later complications or unknown causes	21·6%
Surviving six months or more without anaemia	7·4%
Developing anaemia	19·1%

Deaths within the first month were mostly from leakage or obstruction. Obstruction or perforation still occurred frequently in the later period, but many rats died without the cause being apparent at necropsy.

Post-mortem Findings

At post-mortem examination of animals which have survived the immediate hazards of operation the wall of the cul-de-sac is dilated and hypertrophied, but there is no inflammation or ulceration save in the exceptional case in which rupture has occurred. The tongue, stomach, and the rest of the gut appear normal, as do the other viscera. Histological examination of all these structures shows no departure from the normal. There is some haemosiderosis of the spleen, but the liver and kidneys are normal. Because of the suggestion by Erös (1933) and Jacobson (1939) that the argentaffin cells of the gastro-intestinal tract are concerned in the pathogenesis of the liver-deficiency macrocytic anaemias in man, we paid special attention to these cells in our experimental material and found them normal in appearance, number, and distribution in the stomach and intestine (Cameron, Watson, and Witts, 1950). The nervous plexuses of the gut are normal and there are no abnormalities in sections of the spinal cord. We saw no clinical symptoms of nervous disease even in animals which had been kept alive with folic acid.

The culs-de-sac are usually filled with a thick, dark, liquid material. This consists mainly of the bodies of bacteria with little food residue or desquamated mucosa. The bacteriological findings are much as if the ordinary flora of the caecum had ascended to the loop and the ileum. In the ileum itself there is a great increase in coliform organisms, a decrease in lactobacilli, and a corresponding increase in alpha-haemolytic streptococci.

Post-operative Developments

After operation those rats which do not die from surgical complications in the first few weeks may remain apparently well for long periods. Anaemia develops, often quite suddenly, after an interval which averaged about 90 days in a large series of rats, the range being from 26 days to 6 months. Failure to develop anaemia is sometimes explained by the formation of fistulae or blocking of the loop by adhesions, and similar happenings may account for some of the occasional spontaneous remissions. Nevertheless some animals in which the anatomical stage is set for anaemia do not become anaemic. Quite apart from anaemia, the expectation of life is much diminished in operated rats,

and they not infrequently die for reasons which we do not understand. However, it will be seen from the Table that not many of the rats which survive the initial hazards of the operation will live for six months without developing anaemia. Anaemic animals are perceptibly pale and listless, and may lose weight, but do not show other evidence of disease unless they develop pyogenic infection, to which they are more susceptible than healthy animals. Death may follow within a week of the onset of anaemia, and life is rarely prolonged more than three weeks without treatment, though an occasional anaemic rat has lingered for months and others have had remissions and relapsed again.

The Blood

All blood counts have been done on tail blood, and we have collected a large number of normal data (Cameron and Watson, 1949). The normal haemoglobin of female rats, which we used in all except the earliest experiments, was 13.8 g. per 100 ml. We define anaemia as a haemoglobin value below 10 g., although many of our rats had fallen much below that level before coming under treatment. In a small control series of anaemic rats allowed to die without treatment the haemoglobin at death averaged 5.8 g. per 100 ml., with a range of 2.7 to 8.5 g. per 100 ml. Macrocytosis is always present. In determining the size of the red cells we have relied more heavily on the red-cell diameter, which is a direct measurement, than on the mean corpuscular volume, which includes two sources of error—the red count, and the haematocrit.

From a large series of Price-Jones curves we have established the normal distribution of the red-cell diameter in the rat for our particular technique. The limits of normal for the mean cell diameter in the female rat are 5.73 and 6.56 μ, with an average of 6.14 μ. The normal mean corpuscular volume is 49 μ^3. In anaemic animals the presence of macrocytosis is shown by increase in the mean cell diameter and volume, and by extension of the Price-Jones curve beyond the upper limits of normal. The figures in one small series of 10 anaemic animals averaged 6.62 μ for the mean cell diameter, with a range of 6.37 to 7.33 μ; and 55 μ^3 for the cell volume, with a range of 50 to 67 μ^3. The mean corpuscular haemoglobin is often but not invariably increased.

Macrocytosis is usually obvious in the stained film. Poikilocytosis is never more than slight. The anaemic animals have an irregular reticulocytosis, which may increase from the normal 4% to about 20% as the anaemia worsens, and which is manifested in the stained films by polychromasia. Nucleated red cells are seen in the peripheral blood in all but the lightest anaemias. Leucocytes are not reduced in numbers and they do not show any measurable qualitative change. Marrow smears taken in life show that the cellularity of the marrow is normal or increased (Watson, Cameron, and Witts, 1948). The most striking change is a shift to the left in the maturation of the red-cell precursors. In some cases the increase in proerythroblasts and large basophil erythroblasts is noteworthy, but no cells are seen which correspond exactly with the megaloblasts of human pernicious anaemia.

The serum is crystal-clear and therefore no estimation of serum bilirubin has been attempted. The amount of urobilinogen excreted in the faeces is significantly increased (Badenoch and Watson, 1951). As the normal daily excretion of urobilinogen roughly parallels the amount of haemoglobin in circulation, we have expressed our results in the form of the haemolytic index (Miller, Singer, and Dameshek, 1942). This is the figure obtained by dividing the daily excretion of pigment in milligrams by the total haemoglobin in grammes and expressing this fraction as a percentage. The haemolytic index in the anaemic rats is seven times as high as in the normals. Fat absorption was deficient in most of the operated rats, but many had steatorrhoea without anaemia and a small proportion developed anaemia without showing impaired absorption of fat. In this latter group there did not appear to be any sepsis or haemorrhage to explain the anaemia. Although, therefore, there is some correlation between anaemia and steatorrhoea, it is not absolute. It is probable that both steatorrhoea and anaemia are due to a common cause, and not that steatorrhoea causes the anaemia (Aitken, Badenoch, and Spray, 1950).

Latent Bartonella infection may be activated when rats with intact spleens are fed on deficient diets (Wills and Mehta, 1930), and it was therefore possible that our animals might have developed bartonellosis and anaemia as a result of nutritional deficiency produced by the intestinal lesion. Blood films from anaemic rats never showed the frank infection with Bartonella which is seen after splenectomy in susceptible animals. However, it is impossible to be sure of identifying small numbers of Bartonellae in stained blood films, and further work was necessary to be certain that the anaemia was not caused by bartonellosis. Two measures were taken. The first was to maintain, with rigorous precautions against infection, a stock of Bartonella-free rats. These animals were prepared by operation in the usual way and it was found that anaemia developed as in the earlier experiments. The second measure was to treat a series of anaemic rats with neoarsphenamine, to which *Bartonella muris* is sensitive, and it was shown that the anaemia was not relieved by this therapy (Watson and Witts, 1951a). It is reasonably certain, therefore, that the development of anaemia in these rats is not dependent on Bartonella infection.

Responses to Treatment

A purified liver extract ("anahaemin") was given by intramuscular injection in single doses of 0.1 to 0.4 ml. to 17 rats with macrocytic anaemia after the earlier and milder operation, the self-emptying loop. In 10 rats there was some response to liver, and of the remaining seven which died six had some complication such as infection or perforation. Some of these rats responded on three successive occasions to an injection of liver extract. Response is shown by a reticulocyte crisis, which must be assessed with caution owing to the irregular reticulocytosis produced by the anaemia, and, more significant, by a rise in the number of red cells and in the haemoglobin. Macrocytosis diminishes, though the red cells may not return completely to normal size. These results appeared to us convincing, but we have not been able to get consistent responses to liver treatment in rats prepared by our present more rigorous procedure.

In the next experiment the blood counts of rats which had been submitted to the standard operation—that is, the 3-in. (7.5-cm.) self-filling loop—were checked at weekly intervals, and anaemic animals were assigned in sequence to one of four groups. One of these was a control group, and the others were treated respectively with anahaemin, pteroylglutamic acid, and vitamin B_{12}.

High doses were used, as from early experience it had seemed that these were necessary. We had already found that supplementing the basic diet with 200 μg. of pteroylglutamic acid daily would not prevent anaemia developing, although this amount is well in excess of what is now thought to be the basal requirement (Darke and White, 1950). The material was given by injection three times a week in the following amounts : anahaemin, 0.5 ml.; pteroylglutamic acid, 7.5 mg.; and vitamin B_{12}, 20 μg. This experiment provided clear evidence in favour of pteroylglutamic acid, which prolonged the duration of survival to approximately 80 days as compared with 20 days in the controls. The effects of anahaemin and vitamin B_{12} were not significant statistically (Cameron, Callender, Watson, and Witts, 1949).

In a final therapeutic experiment a series of anaemic rats were treated with " aureomycin " incorporated into the basic diet. This was found to be as effective as folic acid in curing the anaemia and prolonging life in these rats (Watson and Witts, 1951b).

Discussion

A macrocytic anaemia which is usually fatal develops in a proportion of rats which have survived the operation for the formation of a blind loop in the small intestine. Most of these rats have also a mild steatorrhoea, but the correlation between anaemia and steatorrhoea is not absolute and the anaemia does not seem to be sequential to steatorrhoea. Anaemia is not an inevitable result of the operation, and cases of anaemia tend to occur in runs or crops, as if some common initiating factor appeared from time to time. This initiating factor may well be bacterial in nature—indeed, some of our evidence points to this—but it does not appear to be *Bartonella muris*, as the condition has been induced in a Bartonella-free stock and does not respond to neoarsphenamine. Owing chiefly to the high operative and post-operative mortality, the final yield of rats with anaemia is of the order of 20%, and in some series has been as low as 10%. It sometimes happens, therefore, that a fairly large consecutive series of rats are operated upon without anaemia developing. Nevertheless, this technique has been found to produce anaemia by other groups of workers (Broom, Emmet, and Woods, 1949, personal communication ; Jarman and Underhill, 1951), and a similar condition has been produced by excision of the caecum in the rat (Plum, 1950).

The anaemia is of a macrocytic haemolytic character with reticulocytosis and increased pigment excretion. The bone marrow shows a shift of erythropoiesis to the left, but cells comparable to the megaloblasts of pernicious anaemia in man or the primitive erythroblasts of the foetal rat are rarely seen. The anaemia usually responds well to folic acid but not to refined liver extract or to vitamin B_{12}. It also responds to treatment with aureomycin by mouth, and there is a suggestion in the work of Jarman and Underhill (1951) of a response to sulphaguanidine. The anaemia differs from the blood disorder produced in the rat by folic-acid deficiency, which is macrocytic without haemolytic features and in which leucopenia is more prominent than anaemia (Kodicek and Carpenter, 1950). Nor is it identical with the condition produced in the rat by folic-acid antagonists, where the bone marrow has usually been hypoplastic (Oleson, Hutchings, and Subbarow, 1948 ; Philips and Thiersch, 1949), though megaloblastic arrest has been reported once (Franklin *et al.*, 1947), as has also an active non-megaloblastic marrow (Weir, Heinle, and Welch, 1948). Thiersch and Philips (1949) point out that there are wide variations in the response of different species to folic-acid antagonists.

It is not easy to postulate the mechanism by which an intestinal cul-de-sac gives rise to anaemia in the rat, but there is sufficient evidence to permit limited speculation. We know that in these rats there is a bacterial invasion of the small bowel similar to that which occurs in people with gastro-colic fistula, and it is likely that the anaemia and steatorrhoea are similar in nature in the two conditions. The response to aureomycin, which may be presumed to check this invasion, is of particular interest in view of recent reports of the therapeutic value of aureomycin and penicillin in pernicious anaemia in man (Lichtman, Ginsberg, and Watson, 1950 ; Foy, Kondi, and Hargreaves, 1951) and the much older reports on the value of ileostomy in human pernicious anaemia (Seyderhelm, 1924 ; Dixon, Burns, and Giffin, 1925). These observations in rats and in man suggest that the intestinal bacteria have something to do with the absorption or the requirements of vitamin B_{12} and folic acid. Support for this view comes from the work of Davis and Chow (1951), who found that aureomycin increased the vitamin-B_{12} content of the faeces of rats given radioactive cobalt with their diet, measured by both radioactive and microbiological methods.

We have thought that when there is stenosis of the small intestine or a stagnant loop the decisive event in the production of anaemia may be a change in the flora of the loop or the small intestine. There are several ways in which this could lead to anaemia. It might cause the loss of an organism which synthesizes haemopoietic material, or the predominance of an organism which uses up haemopoietic material. It is possible that a toxin is formed which acts other than by interference with the production or absorption of haemopoietic materials. The rapid onset of vitamin-B deficiency in patients who have undergone total gastrectomy suggests that such ideas are not extravagant (Brain and Stammers, 1951), and the production of pernicious anaemia by the fish tapeworm in the small intestine is another parallel (von Bonsdorff, 1948).

It would clearly be desirable to test such ideas by experiment both in man and in animals. Unfortunately the difficulties of detailed microbiological studies in the intestine are considerable, and, owing to the high mortality and frequent post-operative complications, the rat with an intestinal cul-de-sac has not proved an entirely satisfactory pharmacological preparation. We have been unable to diminish the mortality and complications greatly by improvements in technique. They seem to be closely related to the small size of the rat, and it may be necessary to use a larger experimental animal if the anaemia of intestinal stenosis and anastomosis is to be studied further by animal experiment.

Summary

The well-known clinical association of megaloblastic anaemia with intestinal stricture and anastomosis suggested that an operation of this type might be used to produce macrocytic anaemia in an experimental animal.

The formation of a small intestinal cul-de-sac in the rat leads to macrocytic anaemia in a proportion of cases, provided that the cul-de-sac has stagnant contents and is placed in the upper part of the small intestine.

The anaemia is associated with haemolysis, and sometimes with steatorrhoea. It responds well to folic acid or aureomycin but poorly or not at all to vitamin B_{12}.

From the available evidence the most likely cause of the anaemia is an alteration of the intestinal flora analogous to that which occurs in cases of gastro-colic fistula in man, and it is possible that the intestinal bacteria are in some way concerned with the absorption or utilization of haemopoietic substances.

We wish to thank our collaborators, whose names are mentioned in the references, and we are indebted to the Medical Research Council for a grant for technical assistance and expenses.

REFERENCES

Aitken, M. A., Badenoch, J., and Spray, G. H. (1950). *Brit. J. exp. Path.*, **31**, 355.
Badenoch, J., and Watson, G. M. (1951). *J. Path. Bact.*, **63**, 523.
Barker, W. H., and Hummel, L. E. (1929). *Bull. Johns Hopk. Hosp.*, **64**, 215.
Brain, R. H. F., and Stammers, F. A. R. (1951). *Lancet*, **1**, 1137.
Cameron, D. G., Callender, S. T. E., Watson, G. M., and Witts, L. J. (1949). *Nature, Lond.*, **164**, 188.
—— and Watson, G. M. (1949). *Blood*, **4**, 816.
—— —— and Witts, L. J. (1949a). Ibid., **4**, 793.
—— —— —— (1949b). Ibid., **4**, 803.
—— —— —— (1950). *Brit. J. exp. Path.*, **31**, 349.
Castle, W. B., Heath, C. W., and Strauss, M. B. (1931). *Amer. J. med. Sci.*, **187**, 741.
Darke, S. J., and White, C. (1950). *Brit. J. Nutrit.*, **4**, 9.
Davis, R. L., and Chow, B. F. (1951). *Proc. Soc. exp. Biol., N.Y.*, **77**, 218.
Dixon, C. F., Burns, J. G., and Giffin, H. Z. (1925). *J. Amer. med. Ass.*, **85**, 17.
Erös, G. (1933). *Wien. klin. Wschr.*, **46**, 1119.
Faber, K. (1895). *Hospitalstidende*, **3**, 601.
Foy, H., Kondi, A., and Hargreaves, A. (1951). *British Medical Journal*, **1**, 380, 1108.
Franklin, A. L., Stokstad, E. L. R., Belt, M., and Jukes, T. H. (1947). *J. biol. Chem.*, **169**, 427.
Jacobson, W. (1939). *J. Path. Bact.*, **49**, 1.
Jarman, R. M., and Underhill, S. W. F. (1951). *J. Pharm. Pharmacol.*, **3**, 87.
Kodicek, E., and Carpenter, K. J. (1950). *Blood*, **5**, 522.
Lichtman, H., Ginsberg, V., and Watson, J. (1950). *Proc. Soc. exp. Biol., N.Y.*, **74**, 884.
Little, W. D., Zerfas, L. G., and Trusler, H. M. (1929). *J. Amer. med. Ass.*, **93**, 1290.
MacDonald, R. M., Ingelfinger, F. J., and Belding, H. W. (1947). *New Engl. J. Med.*, **237**, 887.
Miller, E. B., Singer, K., and Dameshek, W. (1942). *Arch. intern. Med.*, **70**, 722.
Oleson, J. J., Hutchings, B. L., and Subbarow, Y. (1948). *J. biol. Chem.*, **175**, 359.
Philips, F. S., and Thiersch, J. B. (1949). *J. Pharmacol.*, **95**, 303.
Plum, C. M. (1950). *Sang*, **21**, 437.
Renshaw, R. J. F., Templeton, F. E., and Kiskadden, R. M. (1946). *Gastroenterology*, **7**, 511.
Schlesinger, A. (1933). *Klin. Wschr.*, **12**, 298.
Seyderhelm, R. (1924). Ibid., **3**, 568.
—— Lehmann, W., and Wichels, P. (1924). Ibid., **3**, 1439.
Thiersch, J. B., and Philips, F. S. (1949). *Proc. Soc. exp. Biol., N.Y.*, **71**, 484.
Tönnis, W., Horster, H., Reimers, C., and Rüdel, C. (1932). *Z. ges. exp. Med.*, **84**, 782.
von Bonsdorff, B. (1948). *Blood*, **3**, 91.
Watson, G. M., Cameron, D. G., and Witts, L. J. (1948). *Lancet*, **2**, 404.
—— and Witts, L. J. (1951a). *J. Path. Bact.*, **63**, 526.
—— —— (1951b). In publication.
Weir, D. R., Heinle, R. W., and Welch, A. D. (1948). *Proc. Soc. exp. Biol., N.Y.*, **69**, 211.
Wills, L., and Mehta, M. M. (1930). *Indian J. med. Res.*, **18**, 663.

Nearly 800 new members were recruited in England and Wales to the National Hospital Service Reserve in November, bringing the total strength to 18,573. Of these, 1,706 are trained nurses and 16,839 nursing auxiliaries. Newcastle Hospital Region headed the November recruiting with 200 members, more than a quarter of the month's total of 796. Manchester came second with 102, and Bristol third with 94. Wales still has the largest total membership, 3,634, followed by the South-west Metropolitan Area with 2,277, and Newcastle with 1,643. A new recruiting drive was launched at the end of November by Miss Hornsby-Smith, Parliamentary Secretary to the Ministry of Health, with the aim of trebling membership and so bringing the Reserve well on the way to its peacetime objective of 80,000 members.

THE EFFECT ON BLEEDING-TIME OF AN EXTRACT OF BLOOD OF PATIENTS WITH RHEUMATOID ARTHRITIS

BY

RAYMOND GREENE, D.M., M.R.C.P.
Physician, Royal Northern and Metropolitan Hospitals

JOSEPHINE VAUGHAN-MORGAN, B.Sc.
Formerly Biochemist to the Phillip Hill Clinic at the Royal Northern Hospital

AND

JULIA GAMMON, B.Sc.
Formerly Deputy Biochemist to the Phillip Hill Clinic at the Royal Northern Hospital

It has for many years been a matter of discussion among those interested in the origins of rheumatoid arthritis that the disease may arise in apparent association with a large number of disturbing incidents, including infection, trauma, burns, excessive fatigue, the use of certain drugs, the metabolic crises of puberty, child-bearing, and the climacteric, and the psychological stresses and strains of normal life. That these incidents were the only cause was never believed, and statisticians who disproved to the hilt their sole significance might have excused themselves the labour of belabouring a donkey which had never lived.

Nevertheless, to experienced clinicians it was obvious that, though the majority of people could suffer with impunity the "slings and arrows of outrageous fortune," there were others who could not. Their interest was centred not on the hammer's stroke but on the anvil's ring, and was intensified by the description by Hans Selye (1936b, 1937) of the alarm reaction, which concentrated their attention upon the adrenal cortex. From the beginning it seemed likely, on clinical grounds, that the adrenals, if involved at all in the story of rheumatoid arthritis, would be found to be normal in this condition, for no evidence of adrenal deficiency had been observed in extensive investigations of the biochemistry of rheumatism. It seemed more likely that the error would be found in a mechanism in which the adrenal cortex served as an essential part, and that it would be in the control of the adrenals or in the response to the adrenals that the error would be found.

The Literature

Various Soviet authors (Synovich, 1940; Pshenichnikov, 1940; Novikov, 1941—reviewed by Clarke, 1941) claimed to have shown that the systemic use of local anaesthetics had resulted in a significant decrease in traumatic shock. Their results were confirmed by Ungar (1943), who found that "nupercaine" (cinchocaine) was especially effective. Extending his observations, Ungar (1944) found that several procedures were capable of protecting guinea-pigs and rats against subsequent trauma by causing an inhibition of histamine release. These procedures included the production of previous minor trauma and the administration of ascorbic acid, nupercaine, procaine, cocaine, adrenaline in unphysiological doses, a whole cortical extract prepared by Kendall, anterior pituitary extract, and, pre-eminently, adrenocorticotrophic hormone (A.C.T.H.). The protection afforded by these procedures (except the

administration of ascorbic acid) could be passively transferred in the serum from one animal to another, and was therefore due to a substance contained in the serum.

Inhibition of histamine release and consequent protection could be obtained, however, in adrenalectomized rats only by ascorbic acid and by adrenal extracts. Moreover, the inhibitory substance could not be demonstrated in the blood of hypophysectomized animals. Ungar concluded that certain procedures, including trauma, and the injection of peptone and certain drugs, causes the pituitary to release into the circulation a substance which stimulates the adrenals, which in their turn initiate the production of a protective substance. His results afforded a possible explanation of the observation of many workers that hypophysectomized and adrenalectomized animals are highly sensitive to trauma, and of the fact that the former may be protected by the administration of A.C.T.H. (Reiss, Macleod, and Golla, 1943). Ungar considered that the mechanism he postulated was a part of the alarm reaction described by Selye.

Action of Splenic Extracts

In 1945 Ungar published a further communication in which he claimed to show that the protective substance in question is derived from the spleen, from which it is released under the stimulation of the adrenal cortex. He had previously shown that substances which inhibited histamine release reduced bleeding-time and increased capillary resistance. He selected reduction of bleeding-time as the easiest and most reliable test for the substances involved in the endocrine reaction to trauma, and found that a reduction occurred after trauma in normal rats but not in hypophysectomized rats unless these were treated with A.C.T.H., adrenal extract, or splenic extract. Secondly, the reduction occurred in adrenalectomized rats only if they were treated with adrenal extract or splenic extract. Thirdly, the reduction occurred in splenectomized rats only if they were treated with splenic extract. Similar effects could not be induced with other tissue extracts.

A curious point about the action of some splenic extracts now came to light. Small doses reduced the bleeding-time, but large doses increased it. This anomaly was subsequently found to be due to the presence in the extracts of two substances named by Ungar "splenin A" and "splenin B" (Ungar, 1945, 1946–7), whose pharmacological effects are opposed to one another. "Splenin A" is probably a derivative of ascorbic acid (Ungar, 1946–7), and "splenin B" is an ester of two or three fatty acids with a complex alcohol (Ungar and Damgaard, 1951). Ungar succeeded in demonstrating "splenin B" in human serum in various pathological conditions (purpura, haemolytic jaundice, paroxysmal haemoglobinuria, scurvy, and, at our instigation, rheumatoid arthritis) and from the serum of guinea-pigs after thyroidectomy. We have found it (or a similar substance) in the serum in cases of thyrotoxicosis and rheumatoid arthritis (Greene, 1950), but never in that of healthy persons.

The spleen has been for many years an organ of special interest to students of the rheumatic diseases because of its enlargement in Still's disease and Felty's syndrome. The possible role of the adrenal cortex had attracted a curiously limited attention since the publications of Selye (1936a) had begun. The work of Ungar suggested a possible line of attack, and in 1946 he was kind enough to test a number of unlabelled samples of serum sent to him from the Metropolitan Hospital. Two samples from cases of rheumatoid arthritis contained no "splenin A" but appreciable quantities of "splenin B." Four samples from healthy blood donors contained "splenin A" but no "splenin B." The serum from the

TABLE I.—*Data from Experiment 1 (Saline and Procaine)*

Week	Guinea-pig	Group I: Initial Bleeding-time of Guinea-pigs (Seconds)				Group I: Responding Bleeding-time 20 mins. after 0.4 ml. 10% Procaine S.C. (Seconds)				Group II: Guinea-pig	Group II: Initial Bleeding-time of Guinea-pigs (Seconds)				Group II: Responding Bleeding-time 20 mins. after 0·4 ml. Saline S.C. (Seconds)			
1	B1	115	120	130	120	80	85	95	90	A1	140	125	100	115	135	115	130	105
	B2	115	135	130	125	85	75	120	90	A2	165	115	105	130	105	145	115	125
	B3	125	170	140	140	120	95	110	85	A3	155	130	125	120	160	125	95	120
		1,565				1,130					1,525				1,475			
2	A1	115	160	110	100	110	80	90	90	B1	125	145	165	115	160	100	130	105
	A2	130	145	180	150	90	110	135	110	B2	95	135	95	135	90	110	110	155
	A3	140	115	130	140	100	105	75	75	B3	130	155	120	120	125	120	155	95
		1,615				1,170					1,535				1,455			
3	B1	135	135	150	150	130	85	120	90	A1	120	95	140	120	150	90	160	130
	B2	140	115	125	130	100	95	120	75	A2	130	110	125	95	130	150	130	135
	B3	130	140	100	130	80	105	70	130	A3	160	110	120	145	95	90	150	130
		1,580				1,200					1,470				1,540			
4	A1	150	170	120	110	100	105	125	125	B1	170	140	130	150	165	125	100	155
	A2	150	120	115	140	130	60	120	100	B2	130	90	125	135	165	125	115	150
	A3	115	130	120	100	70	95	95	85	B3	130	155	120	130	90	160	120	100
		1,540				1,210					1,605				1,570			
5	B1	170	160	150	100	140	90	140	110	A1	130	110	100	100	115	130	90	125
	B2	160	100	115	130	95	75	90	90	A2	160	140	150	130	135	180	150	115
	B3	145	120	110	160	140	70	105	90	A3	160	120	110	100	130	120	130	170
		1,620				1,235					1,510				1,590			
6	A1	120	120	130	170	85	85	85	120	B1	160	125	145	100	130	110	130	120
	A2	140	130	110	160	120	90	105	70	B2	140	95	120	100	120	110	140	130
	A3	120	140	130	110	90	105	65	110	B3	165	125	120	80	140	90	150	125
		1,580				1,130					1,475				1,495			
Grand Totals		9,500				7,075					9,120				9,125			
Average Time		132 seconds				98 seconds					127 seconds				127 seconds			

rheumatic patients was tested again after clinically successful treatment with A.C.T.H. and found to contain "splenin A" but no "splenin B" (Greene, 1950).

These results were encouraging, but it was clear that they might be fortuitous. The hypothesis advanced by Ungar rested on a foundation which seemed insufficiently solid—the estimation of bleeding-time in a comparatively small number of guinea-pigs. It was therefore decided to submit his method to a careful experimental trial.

Experiment 1

The first experiments were carried out to find the variation of the normal bleeding-time of guinea-pigs under carefully controlled conditions and the effect on it of a single dose of procaine. The bleeding-time was measured on the ear. Four readings were made, two on each ear, and the average of these was taken as the mean bleeding-time. The ear was pricked with a needle (1 mm. in diameter) and the bleeding observed and the wound blotted at intervals of five seconds. Bleeding was considered to have stopped when no issue of blood or serum could be detected for 10 seconds (Ungar, 1945). Six albino guinea-pigs of the same sex and approximately equal weight were chosen for the experiment. Each week the average bleeding time was measured on three of the animals before and 20 minutes after an injection of 0.4 ml. of 10% procaine, and, as a control, on three before and 20 minutes after an injection of 0.4 ml. of normal saline. This was continued for six weeks, so that both sets of guinea-pigs had alternate injections of procaine and saline. All injections were given subcutaneously. The results are recorded in Table I.

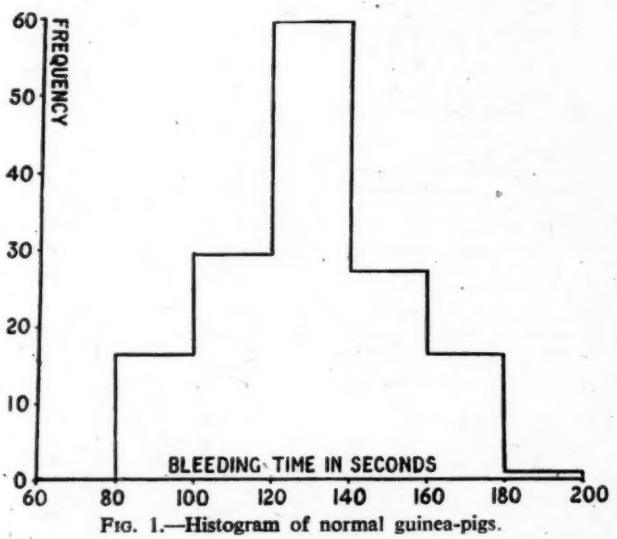


FIG. 1.—Histogram of normal guinea-pigs.

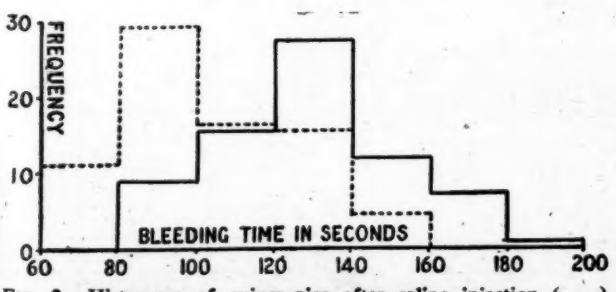


FIG. 2.—Histogram of guinea-pigs after saline injection (——) and after procaine injection (- - - -).

The figures in Table I are expressed as histograms (Figs. 1 and 2). The first shows the variation in bleeding-time of normal guinea-pigs. Out of 144 measurements 77% lie between 100 and 155, with an average of 129 seconds. The form of the distribution is symmetrical and approximately normal. Fig. 2 shows that the measurements after saline injection are fairly similar. Out of 72 observations 76% lie between 100 and 155, with an average of 132 seconds. In contrast, the measurements after procaine injection are very different. Of the observations 79% lie between 75 and 135, with an average of 98 seconds. The histograms in Fig. 2 overlap to the extent of 33%. It is accordingly desirable to have a more sensitive test for a real difference than one based only on the appearance of the histograms.

The data from Table I give the variance analysis shown in Table II, demonstrating that each of the six guinea-pigs has a characteristic bleeding-time (variance

TABLE II.—*Analysis of Variance (Experiment 1)*

Source of Variance	Sum of Squares	Degrees of Freedom	Mean Square	Variance Ratio	Probability
Variation due to characteristic bleeding-times of each guinea-pig ..	5,860	5	1,172	2·87	0.05 to 0·01
Variation due to characteristic day effects on the bleeding-time ..	1,369	5	274	0·67	N.S.*
Interaction of the above effects with each other	5,683	10	568	1·39	N.S.
Effect of procaine compound with all other groups	49,202	1	49,202	120·59	0·001 >
Variation among other groups—e.g., normal groups and saline group	1,320	2	660	1.62	N.S.
Residue remaining after removal of the above effects regarded as error arising randomly† ..	107,731	264	408	—	
Total variation from all sources	171,165	287	—		

* N.S. signifies non-significant in the sense that the differences found are no greater than would be expected to occur by chance. Significance is conventionally regarded as beginning at the once-in-twenty-times level.

† The residue was extensively examined in order to observe other systematic effects. None were found, and it was therefore expressed as a single item.

ratio=2.87, $n_1=5$, $n_2=264$, $0.05>P>0.01$), which persists from day to day (variance ratio=1.39, $n_1=10$, $n_2=264$, not significant). On all six days of the experiment the bleeding-times appear not to have changed (variance ratio=0.67, $n_1=5$, $n_2=264$, not significant). The normal bleeding-times of guinea-pigs do not differ from the bleeding-times after saline injection (variance ratio=1.62, $n_1=2$, $n_2=264$, not significant). The procaine-treated group differ considerably (variance ratio=120.59, $n_1=1$, $n_2=264$, $P=0.001$)—more, in fact, than would be supposed from the histograms, since here the bias of each individual guinea-pig has been eliminated. Clearly, procaine has been effective in reducing the bleeding-time.

Experiment 2

The second set of experiments was designed to compare the effects of serum from normal subjects and from patients suffering from active rheumatoid arthritis, all of whom had an E.S.R. of over 20 mm. in the first hour, measured by Wintrobe's method. In each case the serum was collected, pooled, and freeze-dried in 20-ml. portions and kept until required.

The serum was extracted with chloroform and acetone in order to separate Ungar's chloroform-soluble "splenin A" from the acetone-soluble "splenin

B." For each test 20 ml. of serum was shaken with three 20-ml. portions of chloroform. The combined chloroform extracts were filtered and evaporated to dryness, leaving a residue of "splenin A" and "B." To separate the "splenin B" from the residue, 20 ml. of acetone was added. The acetone was then decanted and evaporated, leaving the dry extract of "splenin B." Just before testing, 2 ml. of saline was added to both residues and 1 ml. per kg. used for injection.

In each case the average bleeding-times of the guinea-pigs were recorded every week, and the day before and one hour after injection. The experiment was continued for twelve weeks, the same guinea-pigs being used as in the previous experiment.

TABLE III.—*Data from Experiment 2 (Normal Serum)*

Week	Group III									Group IV								
	Guinea-pig	Initial Bleeding-time of Guinea-pigs				Responding Bleeding-time 1 Hour after Extract A S.C.				Guinea-pig	Initial Bleeding-time of Guinea-pigs				Responding Bleeding-time 1 Hour after Extract B S.C.			
1	C1	145	110	130	120	120	120	75	65	D1	130	180	125	100	110	135	125	170
	C2	90	130	100	120	110	80	95	95	D2	150	95	165	105	160	120	170	120
	C3	95	140	120	120	110	100	105	100	D3	125	120	120	140	120	100	120	160
		1,420				1,175					1,555				1,610			
2	D1	110	170	120	75	100	120	100	75	C1	160	95	95	175	119	140	90	100
	D2	120	155	100	95	150	150	100	70	C2	110	110	105	130	100	125	125	105
	D3	90	130	165	90	90	90	95	80	C3	160	120	180	100	125	130	130	140
		1,420				1,220					1,540				1,429			
3	C1	120	95	100	180	70	115	135	110	D1	100	100	120	150	130	135	160	85
	C2	110	100	110	90	70	90	85	120	D2	180	130	150	70	180	90	115	125
	C3	140	125	180	100	125	120	110	95	D3	125	120	175	175	180	130	135	100
		1,450				1,245					1,595				1,565			
4	D1	140	90	120	105	125	75	60	80	C1	140	100	130	130	125	110	100	140
	D2	165	105	150	90	85	60	90	150	C2	120	140	130	120	80	130	100	160
	D3	145	120	125	110	140	80	95	100	C3	120	120	105	105	95	125	110	165
		1,465				1,140					1,460				1,440			
5	C1	170	85	120	120	90	105	95	125	D1	140	160	125	110	170	70	120	65
	C2	95	135	120	180	125	145	70	105	D2	180	100	105	135	165	90	65	120
	C3	110	150	90	110	130	155	70	170	D3	180	130	140	95	115	160	90	120
		1,485				1,385					1,600				1,350			
6	D1	145	115	125	150	140	115	125	70	C1	100	150	140	100	90	110	170	105
	D2	120	130	175	80	60	100	85	95	C2	130	95	105	140	80	110	140	150
	D3	100	110	135	115	75	135	90	75	C3	140	100	135	110	160	70	105	130
		1,500				1,165					1,445				1,420			
Grand Totals		8,740				7,330					9,195				8,814			
Average		122 seconds				102 seconds					128 seconds				123 seconds			

TABLE IV.—*Data from Experiment 2 (Rheumatoid Serum)*

Week	Group V									Group VI								
	Guinea-pig	Initial Bleeding-time of Guinea-pigs				Responding Bleeding-time 1 Hour after Extract A				Guinea-pig	Initial Bleeding-time of Guinea-pigs				Responding Bleeding-time 1 Hour after Extract B			
7	E1	125	105	180	120	70	75	140	155	F1	100	125	135	110	200	90	90	175
	E2	110	130	95	160	145	95	100	145	F2	165	110	95	105	125	195	190	140
	E3	120	100	155	100	95	120	145	120	F3	185	135	120	90	210	120	140	135
		1,500				1,405					1,475				1,810			
8	F1	120	130	180	135	180	180	60	90	E1	175	120	135	180	120	125	160	120
	F2	80	130	120	130	155	100	200	60	E2	95	185	145	125	230	180	120	210
	F3	120	175	120	120	100	100	90	120	E3	135	110	175	90	145	165	165	160
		1,560				1,435					1,670				1,900			
9	E1	120	135	105	140	135	110	170	70	F1	135	80	150	135	150	145	180	120
	E2	160	125	85	180	95	110	170	90	F2	130	110	140	135	160	120	140	240
	E3	90	105	180	145	170	110	110	110	F3	120	135	185	95	165	100	180	120
		1,570				1,450					1,550				1,820			
10	F1	96	109	80	100	60	164	118	146	E1	135	134	108	137	157	117	212	150
	F2	118	119	130	145	115	157	125	105	E2	110	120	150	120	120	130	180	215
	F3	150	60	135	108	145	87	95	140	E3	120	145	87	136	145	125	165	166
		1,350				1,457					1,502				1,882			
11	E1	112	120	105	127	180	109	143	135	F1	125	115	95	85	190	120	150	186
	E2	100	110	150	155	150	95	90	96	F2	135	140	180	110	131	125	215	100
	E3	145	100	128	95	150	88	124	126	F3	124	160	151	125	138	219	90	135
		1,447				1,486					1,545				1,799			
12	F1	96	90	125	100	92	66	120	166	E1	123	101	150	160	135	100	154	131
	F2	90	105	130	143	130	78	155	109	E2	90	120	125	135	162	173	103	180
	F3	100	134	120	100	120	102	150	87	E3	111	197	120	95	118	130	144	120
		1,333				1,375					1,527				1,650			
Grand Totals		8,760				8,608					9,269				10,861			
Average		122 seconds				120 seconds					129 seconds				151 seconds			

During the first six weeks each group of three pigs received alternately the saline extracts of "splenin A" and of "splenin B" from pooled normal serum. During the last six weeks they received extracts of "splenin A" and of "splenin B" from pooled rheumatoid serum. The results are recorded in Table III and Table IV.

TABLE V.—*Analysis of Variance (Experiment 2)*

Source of Variance	Sum of Squares	Degrees of Freedom	Mean Square	Variance Ratio	Probability
Variation due to characteristic bleeding-times of each guinea-pig ..	1,403	5	281	0·30	N S
Variation due to characteristic day effects on the bleeding-time ..	7,805	10	781	0.85	N.S.
Variation among each set of four observations taken in sequence ..	401,712	432	936	1·01	N.S
Effects of Treatments:					
Variation among the four groups of guinea-pigs before treatment ..	3,267	3	1,089	1·18	N.S
Decrease in bleeding-time due to:					
Normal serum extract A	13,806	1	13,806	14·96	0·001 > P
Normal serum extract B	1,008	1	1,008	1·09	N.S.
Rheumatoid serum extract A ..	160	1	160	0.17	N.S.
Increase in bleeding-time due to rheumatoid serum extract B ..	17,600	1	17,600	19·07	0·001 > P
Residue remaining after removal of the above effects regarded as error arising randomly ..	111,731	121	923	—	
Total variation from all sources	558,492	575			

The data in Tables III and IV gave the variance analysis shown in Table V. From this it can be seen that the six guinea-pigs were more uniform than those used in the first experiment (variance ratio=0.85, $n_1=5$, $n_2=121$, not significant). The twelve occasions on which the experiment was carried out did not give rise to differences in bleeding-times (variance ratio=0.85, $n_1=10$, $n_2=121$, not significant). The four groups of observations before treatment did not vary more than would be expected ($F=1.18$, $n_1=3$, $n_2=121$, not significant). After treatment with serum extracts the groups differed. Table VI shows the differences,

TABLE VI

Treatment	Initial Bleeding-time	Alteration in Bleeding-time	Responding Bleeding-time
Normal serum extract A	122 seconds	Decreased 20	102 seconds
Normal serum extract B	128 ,,	,, 5	123 ,,
Rheumatoid serum extract A	122 ,,	,, 2	120 ,,
Rheumatoid serum extract B	129 ,,	Increased 22	151 ,,

and from the variance analysis (Table V) it appears that normal serum extract A decreases the bleeding-time (variance ratio=14.96, $n_1=1$, $n_2=121$, $P=0.001$) and rheumatoid serum extract B increases it (variance ratio=19.07, $n_1=1$, $n_2=121$, $P=0.001$). The remaining two treatments were ineffective at the dose given (variance ratio=1.09 and 0.17, respectively, $n_1=1$, $n_2=121$, not significant).

Conclusions

It is concluded that a factor or group of factors present in the "splenin A" extract of normal serum reduces bleeding-time, but is absent from a similar extract from rheumatoid patients. A factor or group of factors is present in the "splenin B" extract of rheumatoid serum that increases bleeding-time, but is absent from normal serum. Both effects have been found consistently.

The experiments, while confirming the existence of the substances called by Ungar "splenin A" and "splenin B," give no indication of the manner or place of production of these substances. His view that they are produced in the spleen and that their production forms part of the general adaptation syndrome is at present under investigation.

We wish to express our thanks to Dr. G. Ungar for initiating us into his methods of extracting the "splenins"; to Mr. A. L. Bacharach and Mr. B. Basil, both of Glaxo Laboratories Ltd., for their help in planning this experiment and undertaking the statistical analysis, respectively; and to Dr. W. J. Martin, of the Statistical Research Unit, London School of Hygiene and Tropical Medicine, for his helpful criticism.

REFERENCES

Clarke, R. (1941). *British Medical Journal*, **2**, 372.
Greene, R. (1950). *Proc. roy. Soc. Med.*, **43**, 16.
Reiss, M., Macleod, L. D., and Golla, Y. M. L. (1943). *Endocrinol.*, **3**, 292.
Selye, H. (1936a). *Nature, Lond.*, **138**, 32.
—— (1936b). *Canad. med. Ass. J.*, **34**, 706.
—— (1937). *Endocrinology*, **21**, 169.
Ungar, G. (1943). *Lancet*, **1**, 421.
—— (1944). *J. Physiol.*, **103**, 333.
—— (1945). *Endocrinology*, **37**, 329.
—— (1946–7). *J. Physiol. Paris*, **39**, 219.
—— and Damgaard, E. (1951). *J. exp. Med.*, **93**, 89.

THE STERILIZATION OF WOOLLEN FABRICS

BY

H. F. BARNARD, M.B., B.S.
Pathologist, Westwood Hospital, Beverley, E. Yorks

Air-borne infection is frequent in the case both of wounds and of infections of the respiratory tract. The infectious organisms are carried on dust or on droplets and droplet nuclei arising from the mouth and nose. Of the two, dust is probably responsible for greater degrees of air contamination (Hare and MacKenzie, 1946; Duguid and Wallace, 1948). Such infected dust arises for the most part from the movement of fabrics—for example, blankets, clothes (van den Ende, Lush, and Edward, 1940; Green, Challinor, and Duguid, 1945; Duguid and Wallace, 1948), bandages (Bourdillon and Colebrook, 1946), and handkerchiefs (Dumbell, Lovelock, and Lowbury, 1948), and to a somewhat less extent from floor-sweeping (Green, Challinor, and Duguid, 1945), although much of this floor dust has come in the first place from fabrics.

Dust-borne bacteria are relatively resistant to the bactericidal action of ultra-violet light and chemical aerosols (Twort, Baker, Finn, and Powell, 1940; Dumbell, Lovelock, and Lowbury, 1948). Correct ventilation can clear the air fairly rapidly (Bourdillon and Colebrook, 1946). To a large extent, however, control has depended upon preventing the release of dust, by oiling in the case of blankets (Thomas and van den Ende, 1941) and floors (van den Ende, Lush, and Edward, 1940), by adequate gowning in the case of clothes (Duguid and Wallace, 1948), and also, of course, by washing.

Relatively little attention has been paid until recently to the adequate bacterial cleansing of the fabrics whence comes so much of the pathogen-bearing dust, though the problem has been appreciated by workers in this field. Bourdillon and Colebrook (1946) state that, "whilst a freshly laundered gown or clean sheet is almost sterile, all woollen or flannel articles must be regarded as infected." Colebrook, Cibson, Todd, Clark, Brown, and Anderson (1944) reported finding haemolytic streptococci in freshly laundered blankets in a hospital and, at the same time, in burns, both organisms being of the same type. A similar experience led here to a convenient way of sterilizing blankets.

Cross-infection and Woollens

For some years efforts have been made to reduce the minor infection of clean wounds and similar cross-infections. Mostly these have been caused by the *Staphylococcus aureus*, the majority of strains in hospital cases being penicillin-resistant. Periodical checking of the staff has always shown that some 50% are nasal carriers of this organism, many of these, too, being resistant strains. However, phage-typing of the organisms recovered from patients and staff, kindly carried out by Dr. V. D. Allison, cast doubt on the direct nurse-to-patient route of spread, as the type in the wound often did not correspond with that found in the nurses in contact. Therefore, when the majority of freshly laundered blankets were found to contain *Staph. aureus*, it became desirable to find a convenient way of sterilizing these and closing this possible route of spread.

Woollens, as we know, shrink in hot water, so that though other fabrics are washed at a temperature lethal to most organisms, woollens are not so treated. As Bourdillon and Colebrook (1946) state: "Whilst clean linen and cotton goods are almost sterile, flannel and woollen goods are in a very different category, since in most laundries they are not heated to a bactericidal temperature." In the present case blankets are churned for 10 minutes at 43° C., and staphylococci in test squares of blanket survive the procedure readily. If a piece of blanket is heat-sterilized and then washed in the machine with the routine ward blankets and thereafter cultured, it is found to have picked up, in what appears to be full measure, the bacterial flora from the other blankets. Evidently transfer of organisms between blankets in the wash readily occurs. It is significant, therefore, that one has found occasionally used blankets to be grossly infected with staphylococci.

Sterilization of Blankets

The poor bactericidal results of laundering methods for woollens have led in recent times to attempts being made to find better ways. Bactericidal temperatures being detrimental to wool, attention has been turned to chemical disinfection.

Van den Ende and Spooner (1941) impregnated squares of fabric by soaking in various bactericidal solutions and, when dry, sprayed them with a culture of haemolytic streptococci or with an infected powder. Later the fabric was shaken over an agar plate or wiped on it. A number of bactericides were tried, but none was considered of practical value. Puck, Robertson, Wise, Loosli, and Lemon (1946) used a similar method, and though the fabric, when dried, retained much of the bactericide, the haemolytic streptococci sprayed on to it could later be recovered by culture. Contact between the two was evidently insufficient, probably owing to the bactericide failing to spread readily over the fibres of the fabric. Rountree (1946) and Rountree and Armytage (1946) found that blankets destroyed bacteria when oiled by the method recommended by Harwood, Powney, and Edwards (1944). The bactericidal agent was the detergent cetyl pyridinium bromide (C.P.B.), which remained with the oil in the blanket. Haemolytic streptococci sprayed on to the treated fabric could not be recovered later by wiping it on agar or by washing it in broth. The fabric was not harmed in any way by the process, nor were a small group of people found to be sensitive to contact with the impregnated fabric.

Dumbell and Lovelock (1949) have studied disinfectants suitable for impregnating handkerchiefs to render them self-disinfecting. *Staph. aureus* in saliva was soaked into the treated cotton fabric, which, when dry, was shaken over agar plates. The most active agent tried, hexyl resorcinol, was of prohibitive cost, but octyl cresol and "alkyl" resorcinol were considered practicable. They considered that for handkerchiefs C.P.B. was unsuitable, as it had been reported by Williams, Clayton-Cooper, Duncan, and Miles (1943) that some people (under 1%) are sensitive to its local application.

Vaughan, Sotier, Hill, Simpson, and Lee (1948) examined ways to sterilize woollens in a laundry wash process. In this work there was no attempt at impregnation to render the fabric self-disinfecting. Chlorination was considered the most practical method, and the agent causing the least harm to dyes and fabric was sodium benzene sulphone chloramide ("monochloramine B"). This method was found suitable for the large-scale treatment of clothing in the American Army. Small fabric squares infected with *Bact. coli* and *B. subtilis* were included with the clothing treated, and were afterwards found to be sterile.

Before we became acquainted with the above relevant literature, consideration had been given to chemical disinfection of blankets. For reasons of cost, toxicity, damage to fabric, and so on, all but a few disinfectants appeared to be unsuitable. Trial use was made of calcium hypochlorite in the form of eusol powder over a period of some months, pending the discovery of a better way. It was, in the strength used (2.5% of eusol powder), less adequately bactericidal in the laundry than in the test-tube and, moreover, it produced slight but noticeable hardening of the wool.

C.P.B. seemed to deserve further consideration. It is a cation-active detergent, and as "fixanol C" is manufactured by I.C.I. The high bactericidal activity of certain of the surface active agents has been extensively examined since the publication of Domagk (1935). Quisno and Foter (1946) examined cetyl pyridinium chloride and found it unusual in being highly bactericidal over a wide range of *p*H. Van den Ende, Edward, and Lush (1941) had tried C.P.B. and found that, though it left the fabric bactericidal, it gave a "harsh texture and unpleasant odour." Rountree found fixanol in solution highly bactericidal, especially to Gram-positive organisms. She found that blankets soaked with oil and fixanol solution and dried were virtually sterile for many weeks: 1 in 800 in the blanket (in addition to the oil) was adequate, but 1 in 1,600 was much less so. Patch tests with 1% solution gave no reactions in 17 people.

The purpose of the oiling is to reduce dust release, and, while Rountree (1947) found that it brought no

reduction in surgical cross-infection, Wright, Cruickshank, and Gunn (1944) were able to show a reduction in cross-infection in measles wards. The process, however, is not without disadvantages. It is not very easy for a normal laundry to control, it is somewhat expensive, and the finished product is a slightly oily blanket—though the work of the U.S. Navy Medical Research Unit (1946) would seem to have overcome much of the trouble and cost. It seemed, however, that a trial of fixanol C without oil would be worth making.

Present Investigation

The concentration necessary was suggested by the above oil and fixanol experiments—namely, one part by weight of undiluted fixanol to 800 parts by weight of blanket. It was found that, in the laundry after hydro-extracting, the water held in a blanket before air-drying averages one-third of its dry weight, a gain in weight of 33%. Thus, to attain a final 1 in 800 the blanket would have to be washed in a 1 in 200 solution of fixanol in water and dried without rinsing. The bactericidal effect of different concentrations was tested, the blankets being shaken over blood-agar plates. With this method of culture the number of particles released varies according to the state of the blanket, but it parallels roughly the dispersal of particles in bed-making. Ludlam's medium (Ludlam, 1949) and Chapman's salt agar (Chapman, 1945, 1949) were tried as selective media for staphylococci. The latter was found of some value in this work, but blood agar remained the principal medium. No growth was obtained with final dry concentrations up to 1 in 1,600, and at 1 in 6,400 growth was much reduced and no staphylococci were found (Table and Fig. 1).

Blankets After Treatment with Various Concentrations of Fixanol

	Concentration of Fixanol in Dry Blanket				
	1 in 800	1 in 1,600	1 in 3,200	1 in 6,400	0
No. of colonies on agar ..	±	0	+	++	++++
Size of inhibition zones on staph. spread plate	++++	++	+++	+	0

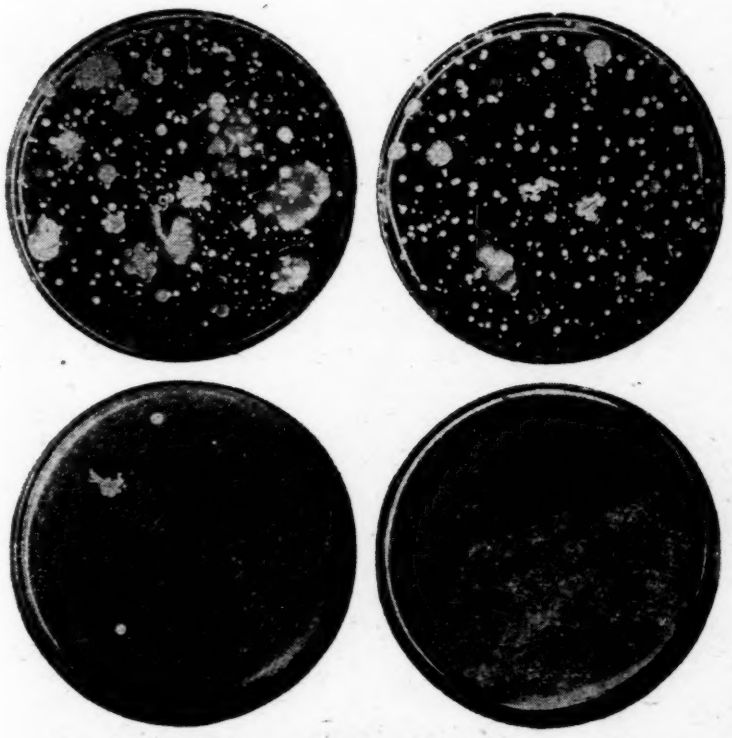


FIG. 1.—Sterilization of blanket with fixanol C. Above: untreated. Below: treated.

The fixanol on the dried blanket coats the individual fibres and readily passes again into solution on contact with moisture. This can conveniently be demonstrated by shaking the treated blanket over a plate which has been freshly spread with *Staph. aureus* broth culture and dried. After incubation, as may be seen in Fig. 2, each fibre is surrounded by a narrow zone of inhibition where no growth has occurred. The concentration of fixanol forming in secretions that reach the blanket will depend upon the volume of secretion and the way it spreads amongst the fibres. A droplet of saliva on a treated blanket examined under a hand lens can be seen to spread to a limited extent (Fig. 3). It is reasonable to suppose that in such a droplet the strength of fixanol lies much above the minimum lethal concentration for staphylococci, which is 1 in 200,000, and even above that for the Gram-negative bacilli, 1 in 1,000. For routine use 1 in 6,400 dry content was chosen. As a check a 1 foot square (0.093 m.²) of blanket was heavily infected in a diluted broth culture of staphylococci, dried, and then washed with 16 other blankets in this chosen concentration. Shaken over blood agar before treatment, the square grew a shower of staphylococci, but afterwards none at all. Further, a blanket that had been treated was some weeks later infected with staphylococcus as above, dried, and shaken over agar. This also grew no staphylococci.

FIG. 2.—Inhibition zones around wool fibres coated with fixanol C.

The same procedures were carried out with *Pseudomonas pyocyanea*, an organism which, with the exception of the tubercle bacillus, is probably the most resistant pathogen to this bactericide as to so many others. There was, as with the staphylococcus, complete failure to recover any of the test organisms when the blanket was infected before being treated with fixanol. When, however, a culture of *Ps. pyocyanea* was sprayed on to or soaked into a blanket square impregnated with fixanol in the usual strength, it was readily recovered later. The same applied even when the concentration of fixanol was raised four times. Evidently, in such absorbed fluids, the concentration of fixanol does not reach the lethal level for Ps. pyocyanea.

Thus, with this procedure the blanket leaves the laundry virtually sterile. Moreover, it will apparently retain, for a considerable period, sufficient material to destroy any staphylococci that may be picked up in secretions. The cost of the detergent is approximately 1d. a blanket, and the procedure is straight-

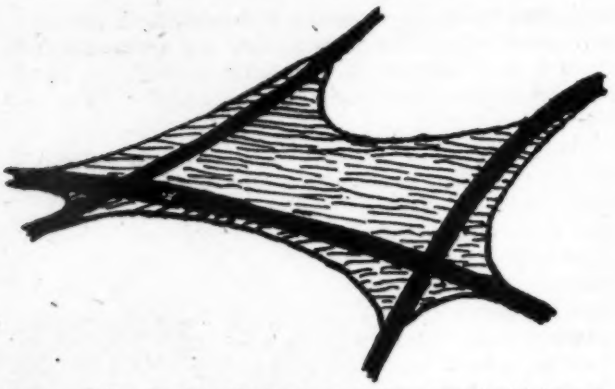


FIG. 3.—Saliva droplet adhering to wool fibres coated with fixanol.

forward. The impregnated blanket has a slightly smooth feel, it has no smell, and in routine hospital use for all blankets for a year there has been no indication of patients showing sensitivity to the treated blankets.

Discussion

The much higher frequency with which penicillin-resistant strains of staphylococci are recovered from hospital cases, as compared with those at home, is largely referable to cross-infection (Rountree and Thomson, 1949; Barber, Hayhoe, and Whitehead, 1949). Nasal carriers of such strains among hospital staff are also frequent, and there is a tendency for newly arrived nurses to acquire the prevailing phage type. Though staff may directly infect patients, both might, as postulated by the *Lancet* (1949), be infected by the hospital environment. The nose is an effective dust filter (StClair Thomson and Hewlett, 1896). This is by virtue of air turbulence and impaction of particles against the moist walls. Thus a ward nurse has something in common with a slit sampler.

It was of interest, therefore, to sterilize the hospital blankets for a period and to observe the effect on the incidence of carriers, and also of cross-infected wounds. Briefly, it may be reported that in three months there was no reduction in the carrier rate, while for wounds the small numbers left the matter in doubt, a certain amount of cross-infection still continuing. No doubt, as observed by Girdlestone, Bourdillon, and McFarlan (1951), there are a multiplicity of sources of infection. A wider trial is desirable in which the sterilization of clothes and other fabrics deserves consideration.

Whilst uncertainty remains on many points, it is not without importance that, as many have observed, pathogens are surviving for long periods in the woollen fabrics of our most immediate environment, and, moreover, that perhaps now this need no longer be so.

Summary

Cross-infection of wounds in a hospital has been investigated. Attention is directed to dust from blankets. From freshly laundered blankets *Staph. aureus* was frequently obtained, which organism readily survived the laundry process. During laundering bacteria pass from one blanket to the next.

Impregnation with cetyl pyridinium bromide (fixanol C) has been found a satisfactory way of sterilizing blankets. They remain, to a large extent, self-disinfecting.

I am indebted to Dr. W. H. James, medical superintendent of the Westwood Hospital, Beverley, for his valuable observation and advice on the clinical aspects; to Dr. W. Goldie, pathologist to St. James's Hospital, Leeds, for his most helpful criticism of the manuscript; and to Mr. A. Manby, senior technician, Westwood Hospital, Beverley, for preparation of the photographs.

REFERENCES

Barber, M., Hayhoe, F. G. J., and Whitehead, J. E. M. (1949). *Lancet*, **2**, 1120.
Bourdillon, R. B., and Colebrook, L. (1946). Ibid., **1**, 561.
Chapman, G. H. (1945). *J. Bact.*, **50**, 201.
—— (1949). Ibid., **58**, 823.
Colebrook, L., Gibson, T., Todd, J. P., Clark, A. M., Brown, A., and Anderson, A. B. (1944). *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 249.
Domagk, G. (1935). *Dtsch. med. Wschr.*, **61**, 829.
Duguid, J. P., and Wallace, A. T. (1948). *Lancet*, **2**, 845.
Dumbell, K. R., and Lovelock, J. E. (1949). Ibid., **1**, 777.
—— —— and Lowbury, E. J. (1948). Ibid., **2**, 183.
Girdlestone, G. R., Bourdillon, R. B., and MacFarlan, A. M. (1951). Ibid., **1**, 597.
Green, C. A., Challinor, S. W., and Duguid, J. P. (1945). *Ann. rheum. Dis.*, **5**, 36.
Hare, R., and MacKenzie, D. M. (1946). *British Medical Journal*, **1**, 865.
Harwood, F. C., Powney, J., and Edwards, C. W. (1944). Ibid., **1**, 615.
Lancet, 1949, **2**, 518.
Ludlam, G. B. (1949). *Mon. Bull. Minist. Hlth*, **8**, 15.
Puck, T. T., Robertson, O. H., Wise, H., Loosli, C. G., and Lemon, H. M. (1946). *Amer. J. Hyg.*, **43**, 91, 105.
Quisno, R., and Foter, M. J. (1946). *J. Bact.*, **52**, 111.
Rountree, P. M. (1946). *Med. J. Aust.*, **1**, 539.
—— (1947). Ibid., **1**, 427.
—— and Armytage, J. E. (1946). Ibid., **1**, 503.
—— and Thomson, E. F. (1949). *Lancet*, **2**, 501.
Thomson, StClair, and Hewlett, R. T. (1896). *Lancet*, **1**, 86.
Thomas, J. C., and van den Ende, M. (1941). *British Medical Journal*, **1**, 953.
Twort, C. C., Baker, A. H., Finn, S. R., and Powell, E. O. (1940). *J. Hyg., Camb.*, **40**, 253.
U.S. Navy Medical Research Unit No. 1 (1946). *Science*, **104**, 60.
van den Ende, M., Edward, D. G. ff., and Lush, D. (1941). *Lancet*, **1**, 716.
—— Lush, D., and Edward, D. G. ff. (1940). Ibid., **2**, 133.
—— and Spooner, E. T. C. (1941). Ibid., **1**, 751.
Vaughan, T. H., Sotier, A. L., Hill, E. F., Simpson, J. E., and Lee, W. M. (1948). *Industr. Engng Chem.*, **40**, 2054.
Williams, R., Clayton-Cooper, B., Duncan, J. Mck., and Miles, E. M. (1943). *Lancet*, **1**, 522.
Wright, J. Cruickshank, R., and Gunn, W. (1944). *British Medical Journal*, **1**, 611.

BACTERIOLOGY OF VAGINAL FLORA AFTER USE OF INTERNAL TAMPONS

BY

ELIZABETH N. BRAND, M.D., D.P.H.

The vaginal tampon is being used with increasing frequency for the absorption of the menstrual flow, but this subject has received little attention from the medical profession in this country, though there still may be a fair amount of prejudice against its use.

Correspondence for and against it appeared in the *British Medical Journal* (1938, 1939). For over 14 years Partridge (1939) had advised its use amongst her patients without there being any complaints or untoward results. Barton (1942) reported on the advantages of intravaginal tampons as menstrual guards.

The matter has been investigated fully by gynaecologists in the U.S.A. Sackren (1939) carried out an investigation on 21 patients and found no irritation in the vaginal or cervical tissues after the use of internal tampons. Thornton (1943) investigated 110 subjects for one to two years and arrived at the same conclusion. Karnaky (1941, 1943) claimed beneficial results in cases of sterility. Magid and Geiger (1942) investigated the bacterial flora in the vagina and cervix after the use of tampons in 25 women, over two menstrual periods,

and could find no appreciable difference. Baba (1946) studied the effect of intravaginal tampons on cervical erosions and vaginal discharges in 55 cases and concluded that, in the majority, their use had a favourable effect.

Genell and Lysander (1939) reported three cases of vaginitis which they attributed to the use of vaginal tampons. The report fails to give previous histories or the length of time the tampon was worn.

Present Investigation

This investigation was mainly concerned with the bacteriology of the vaginal flora following the use of the internal tampon. It was undertaken at the request of the visiting gynaecologists to the Elizabeth Garrett Anderson Hospital and with their co-operation. The object was to obtain information which could be given to patients, nurses, and doctors.

The original intention was to examine 100 volunteers over three monthly periods. Each volunteer was to undergo a pelvic examination by the gynaecologist before and at the end of the three months' use of vaginal tampons. In addition a vaginal swab was to be examined before and after each menstrual period for *p*H, bacteriology, and glycogen content, and to exclude any trichomonal or monilia infection.

Most of the volunteers were obtained from the gynaecological out-patient department, and, as many of these women were either fully employed during the day or were married, with young children, it was found impossible to get them to attend six times in three months. Thus in some cases a swab was taken before the first period and after three successive periods; but pelvic examination was made by the gynaecologist before and after completion of the study. Tampons were given to each subject, and complete instructions on their use were enclosed in each carton.

As these women were not quite normal, it was decided to enrol a number of normal women so that the results could be compared. I am indebted to Dr. Mary Barton for her co-operation, as she enlisted the help of a number of her patients, most of whom attended regularly over three months.

Since this investigation was started (over 13 months ago) 122 volunteers have been enrolled; 57 of these have completed three monthly periods or more, 17 have completed two monthly periods, and 26 have completed one monthly period; 22 have defaulted, 3 through failure to insert the tampon. In all, 100 volunteers completed one cycle or more. Six patients became pregnant.

Most of the volunteers were cases of infertility or dysmenorrhoea. A few had had small cervical erosions or complained of vaginal discharge. Only three of the cases showed a severe vaginitis; these are dealt with separately. Two volunteers were enrolled in rather unusual circumstances. The first reported at hospital thinking she had left a tampon in the vagina since her last menstrual period, over two weeks previously. This was incorrect. The second came with a complaint of offensive vaginal discharge, and on examination was found to have a retained tampon, which had probably been there since her last period three weeks before. In the hands of a careless person this is a possibility which is not likely to occur during the period, as the pad when saturated fails to fulfil its function, but, as quoted by Russell (1939), may occur at the end of the period.

All the volunteers were active women between the ages of 21 and 45 years. Eleven were single and 89 were married; 31 had not used tampons before; 69 had used them, but not all regularly.

The hospital patients suffering from cervical erosions or vaginitis were treated by the gynaecologists. Two swabs were taken on each occasion by rotating the swab round the anterior and posterior wall in the upper part of the vagina. One swab was used for estimating the *p*H by means of Johnson's *p*H papers, and then immersed in normal saline and incubated for a short time to be examined for monilia or trichomonads. The other swab was used for aerobic and anaerobic culture, and films were made for Gram stain and glycogen estimation. The glycogen content was examined by the method recommended by Siegler (1944), and was recorded as a percentage of the epithelial cells containing glycogen.

Bacteriology

Of the 100 volunteers, 63 showed no pelvic abnormality and were regarded as normal for the purposes of this study. One volunteer attended regularly for 10 menstrual periods, two for seven periods, and the rest for periods varying from one to four in number. The predominant organism found in the direct smear from 57 cases in this group was Döderlein's bacillus. The cultures gave a mixed growth of Döderlein's bacillus, coagulase-negative *Staphylococcus albus*, diphtheroid bacilli, and, occasionally, coliform bacilli. The bacteriology was very similar in the pre- and post-menstrual cultures. The remaining six volunteers in this group had an abnormal flora: four showed the presence of *Candida albicans* in direct smear and on culture, one had a persistent growth of a coliform bacillus associated with *Streptococcus faecalis*, and the sixth developed a trichomonal infection with vaginitis. The last-mentioned patient developed an irritating vaginal discharge one week before her second menstrual period, due to *Trichomonas vaginalis*. This was a recurrence of a previous infection. It cleared very quickly with acetarsol pessaries, and did not recur after her next menstrual period.

The four patients with *C. albicans* had no signs or symptoms of vaginitis (yeasts are sometimes found in the healthy vagina), and responded well to "mycil" pessaries in two cases, the flora returning to normal after treatment. The other two cases were not treated, and the infection was uninfluenced. The volunteer whose cultures gave a growth of a coliform bacillus showed no signs of vaginitis or cervicitis, and the flora remained abnormal throughout the investigation. In order to compare the results, post-menstrual swabs were taken from a number of normal young women who used the perineal pad for protection. The bacterial flora thus obtained showed no marked variation from that obtained in the tampon series.

The other 37 volunteers showed some evidence of pelvic disease. Thirty-three had a cervical erosion or showed signs of vaginitis, two had a minor degree of prolapse, one a cystic ovary, and another a fibroid uterus. The majority of the erosions were small and did not require treatment. The larger ones were cauterized at the beginning of the investigation, and some of them were subsequently painted with "negatol" 100%. Three cases, summarized below, showed a severe vaginitis. The bacteriology in the cases of simple erosion corresponded to a normal flora in 20 cases and an abnormal

flora in 10. Of the latter four showed *C. albicans* on smear and culture, one *Tr. vaginalis*, and two coliform bacilli and *Str. faecalis*. The three others have been classified as severe vaginitis. Three of the cases of infection with *C. albicans* were treated; owing to illness the fourth attended during one menstrual period only. Two of the cases responded to treatment, and the infection did not reappear during the investigation. The fourth case did not respond to treatment: this patient had been attending hospital for several months with a chronic vaginitis, and her condition was uninfluenced by the use of vaginal tampons. One negative swab followed treatment of the trichomonal infection with acetarsol pessaries, but the infection recurred six weeks later, after an illness. She was then treated with acetarsol impregnated tampons, and the vaginitis cleared up completely; it had not recurred two months later.

The vaginal *p*H of the cases varied from 4.2 to 5.4, but showed no marked difference in the post-menstrual period.

The glycogen content of the epithelial cells remained fairly constant in all cases. It was normal in some throughout, and low in others, especially in cases of infertility, but was uninfluenced by the use of the tampons.

Case Reports

The following is a summary of the three cases of severe vaginitis mentioned above in which vaginal tampons were used during the menstrual periods, over three months in Cases 1 and 3 and two months in Case 2.

Case 1.—This patient, aged 30, had used vaginal tampons for one year. She complained of an irritating vaginal discharge of one week's duration. Examination revealed a purulent discharge, with severe vaginitis but no erosion. The wet film from the pre-menstrual swab showed many pus cells, hyphae, and spores of monilia. Culture yielded a growth of *C. albicans*, a coliform bacillus, and *Str. faecalis*. The *albicans* infection responded to mycil pessaries, but the coliform infection was still present at the end of the second menstrual period. This was treated with "sulphatriad" pessaries for 10 days, and when the patient returned for her third pre-menstrual swab 11 days after her last treatment the flora had returned to normal, and remained so in her post-menstrual swab. A vaginal examination at this time showed that the vagina and cervix were healthy, and the patient was discharged.

Case 2.—The patient, aged 23, had used vaginal tampons regularly. She complained of an irritating offensive vaginal discharge of three weeks' duration. On examination per vaginam a retained tampon was found which had caused severe vaginitis and a cervical erosion. Unfortunately a swab was not taken. She was advised to douche and return in one week's time. She did not return until 14 days later, as her menstrual period had occurred, during which she had used vaginal tampons. Her discharge was then less offensive, and the vaginitis had abated. A swab taken yielded a mixed growth of a coagulase-positive *Staph. aureus*, coliform bacilli, and *C. albicans*. Treatment consisted of ichthyol and glycerin pessaries and douching. Three weeks later her pre-menstrual swab showed a scanty growth of *C. albicans*, but on examination there was no evidence of vaginal thrush. The post-menstrual swab one week later showed a normal flora. The vaginitis was much improved, the erosion had practically healed, and she had no complaints. Unfortunately this investigation finished at that time, but she was advised to return if her symptoms recurred. She had not done so three months later.

Case 3.—The patient, aged 42, had used vaginal tampons regularly. She complained of excessive loss at periods and vaginal discharge. Examination per vaginam showed a cervical polyp and cervical erosion with vaginitis. The polyp was removed and the erosion cauterized. Two months later this patient volunteered for the investigation. A large erosion was still present. A pre-menstrual swab yielded a growth of a coagulase-negative *Staph. albus* and *Bact. coli*. The erosion was painted with negatol 100%. Her second post-menstrual swab yielded a moderate growth of a coliform bacillus, but on examination the erosion was healing and smaller in size. The third post-menstrual swab showed a normal flora, and the erosion was almost healed.

These three cases responded to active treatment during the three months' investigation. Their progress compared very favourably with four similar cases in which the perineal pad had been used for protection.

Discussion

The principal organism associated with the healthy vagina is a pleomorphic non-sporing Gram-positive bacillus, variably anaerobic, identified by Döderlein in 1892. The vaginal flora found in the healthy adult is mixed, and staphylococci, enterococci, coliforms, and diphtheroids are also present (Wilson and Miles, 1946). Three grades of "cleanliness" are generally recognized in the vagina of the adult, and the classification of Heurlin (1941) is the one most usually accepted (Baird, 1950).

Grade 1.—Many epithelial cells, an occasional leucocyte, many Döderlein bacilli, and hardly any other organisms; *p*H 4–4.6.

Grade 2.—Pus cells in excess of epithelial cells, few Döderlein bacilli, and a mixture of diphtheroids, cocci, and coliforms; *p*H 4.5–6.

Grade 3.—Many pus cells, a few epithelial cells, no Döderlein bacilli. A host of other organisms—Gram-positive and Gram-negative cocco-bacilli, coliforms, Gram-positive bacilli, comma bacillus, and others; *p*H above 6.

Heurlin mentions 37 varieties of bacteria which find their natural habitat in the genital tract. Many of these are saprophytic, and are seen only in direct smear. This may be accounted for by the bactericidal action of the vaginal secretion. With such a variety of organisms found naturally, the criterion adopted for the normal in this study has been the preponderance of Döderlein's bacillus found in smear and on culture; the criterion for the abnormal has been the excess of pus cells and organisms other than Döderlein's.

The organisms found in the post-menstrual cultures of the normal volunteers (63 in number) corresponded mainly to the Grade 1 flora. No appreciable difference was found in the bacterial flora of the pre- and post-menstrual culture. Döderlein's bacillus was the predominant organism in the direct smear, and grew well on culture, especially under anaerobic conditions. It was frequently associated with a coagulase-negative *Staph. albus*, and occasionally with diphtheroid bacilli and a scanty growth of coliform bacilli. Grade 2 flora was found in five cases, four of which showed a monilia infection on culture, and the fifth had a recurrence of a chronic trichomonal infection. In these five cases the pus cells were in excess of the epithelial cells, but in three of them the flora returned to grade 1 after treatment; in two untreated cases it was unaltered.

The bacteriology of the 33 cases with cervical erosions or vaginitis corresponded to grade 1 (20 cases) and grade 2 (10 cases). Three cases of severe vaginitis showed a grade 3 flora.

An anaerobic streptococcus was found on several occasions, but this organism is a normal inhabitant of

the vagina (White, 1933). One strain was sent to the Streptococcal Reference Laboratory at Colindale, and the following report was received: "The streptococcus produced an α-haemolysis, was not heat-resistant, did not belong to any of the Lancefield groups, and formed no mucoid colonies on sucrose agar. It could not be identified."

The anaerobic streptococcus isolated by White was a strict anaerobe, and very slow-growing, requiring two to four days' incubation. None of these organisms was isolated, probably because the cultures became overgrown by contaminants if incubated longer than 48 hours. No gas was formed by any of the anaerobic streptococci, mannite was not fermented, the organism did not grow on MacConkey's medium, and there was no evidence that this organism was pathogenic. *Str. faecalis* was found in association with coliforms on three occasions. In one case the cervix and vagina appeared healthy.

Ten cases were found to have *C. albicans* on culture; only four of these had a vaginal discharge or showed evidence of vaginal thrush. Six cases had no symptoms. Two volunteers had a trichomonal infection: one was a recurrence of a previous infection during the period under study, but it cleared up very quickly with acetarsol pessaries, and did not occur after the next menstrual period. The other was a recent acute infection. None of the other volunteers acquired monilia or trichomonal organisms during the period of study or developed erosions or vaginitis as a result of using the internal tampon.

Erosions

The findings have already been summarized. There was no aggravation of the condition or delay in healing following the use of tampons in the patients who had cervical erosions. All the erosions were reduced in size if not completely healed, and the bacterial flora, where abnormal, had returned to normal at the end of the period under study. The vaginal tampon, when properly used, is not in contact with the cervix but only with the vaginal wall, which is self-protecting (Cruickshank and Sharman, 1934). Three cases had signs of severe vaginitis and one of them had a large erosion, the vaginitis in one case being caused by a retained tampon. They were medically treated by the gynaecologist, and all continued to use tampons for protection. In each case the underlying cause responded to treatment, and did not recur, which proves that the internal tampon does not act as an irritating foreign body. All had a grade 3 flora at the beginning of the study; this reverted to grade 1 at the end. The rate of healing compared favourably with four control cases in which the perineal pad was used.

The glycogen content was estimated as a percentage of the epithelial cells in the smear containing glycogen. It was found to be low in some cases of infertility, but was uninfluenced by the use of tampons. Normally most of the epithelial cells should contain glycogen.

The *p*H was less acid than the normal grade 1 flora in some of the patients, probably owing to the fact that the swab was taken from the upper part of the vagina, to avoid contaminants found in the lower part. There was no appreciable alteration in the *p*H in the pre- and post-menstrual phases.

The volunteers who had not previously used tampons stated that they were comfortable to wear and did not cause the irritation usually found with the perineal pad. A few complained that they did not give enough protection at the beginning of the menstrual period, and that a perineal pad was required as well. There were no complaints of an excessive flow of blood on withdrawal, of difficulty in removal, or of any odour associated with their use. The average number employed in one cycle was ten. Two volunteers stated that they required 15–18 tampons.

Summary

A series of 100 women used vaginal tampons for protection during the menstrual period over three to ten successive periods in 57 cases, two-monthly periods in 17 cases, and one-monthly period in 26 cases. Smears and cultures taken before and after each period showed no appreciable change in the bacterial flora of the vagina.

A study was made of 33 unselected cases of cervical erosion or vaginitis in which internal tampons were used. Healing of the erosions was not adversely affected; it compared favourably with a control series using the perineal pad. In three of the cases the bacterial flora corresponded to grade 3 at the beginning of the study, but returned to the normal grade 1 at the conclusion.

There was no evidence of local irritation or inflammation caused by the use of internal tampons. No appreciable alteration in the vaginal *p*H or in the glycogen content of the epithelial cells was noted. A retained tampon may cause damage to the vagina or cervix, and patients should be warned to remove the soiled one before inserting a fresh one. Removal is particularly important at the end of the menstrual period.

There was no evidence that vaginal tampons are prejudicial to health.

My thanks are due to the gynaecologists of the Elizabeth Garrett Anderson Hospital, in particular to Miss Josephine Barnes for her great help and encouragement throughout the study, and for her most useful criticism of this paper. Tampax Limited aided the research work by a grant, and supplied the tampons.

References

Baba, G. (1946). Address to Obstet. Gynec. Conf., February 21, in Chicago, Illinois.
Baird, D. (1950). *Combined Textbook of Obstetrics and Gynaecology*, p. 1053. Edinburgh.
Barton, M. (1942). *British Medical Journal*, **1**, 524.
British Medical Journal, 1938, **2**, 1113, 1229, 1282.
—— 1939, **1**, 36; **2**, 143, 308.
Cruickshank, R., and Sharman, A. (1934). *J. Obstet. Gynaec. Brit. Emp.*, **41**, 224.
Genell, S., and Lysander, A. (1939). *Svenska Läkartidn.*, **36**, 2236.
Heurlin, M. (1941) Cited by Baird (1950).
Karnaky, K. J. (1941). *Med. Rec. S. Antonio*, **35**, 851.
—— (1943). *West. J. Surg. Obstet. Gynec.*, **51**, 150.
Magid, M. O., and Geiger, J. (1942). *Med. Rec.*, **155**, 316.
Partridge, E. J. (1939). *British Medical Journal*, **1**, 36.
Russell, V. (1939). Ibid., **2**, 143.
Sackren, H. S. (1939). *Clin. Med. Surg.*, **46**, 327.
Siegler, S. L. (1944). *Fertility in Women*, p. 175. Philadelphia.
Thornton, M. J. (1943). *Amer. J. Obstet. Gynec.*, **46**, 259.
White, E. (1933). *J. Obstet. Gynaec. Brit. Emp.*, **40**, 630.
Wilson, G. S., and Miles, A. A. (1946). In Topley and Wilson's *Principles of Bacteriology and Immunity*, 3rd ed. London.

The Ministry of Health is lifting the 21-year-old ban on importing parrots, as from January 8. The regulations have been revoked because there has been no significant recurrence of psittacosis in this country since the world-wide outbreak which led to the ban. Furthermore, research has since shown that psittacosis, which was originally believed to be confined to the parrot species, also occurs in seagulls, pigeons, ducks, turkeys, and similar birds. Moreover, modern drugs, such as penicillin and the new antibiotics, have largely robbed the disease of its dangers. Only one death has occurred in England and Wales in the last 10 years. The lifting of the ban does not affect any other legal requirements. For example, anyone importing a parrot from certain countries will still need a Board of Trade licence to import a seed-eating bird.

A T-PIECE TECHNIQUE FOR GENERAL INHALATIONAL ANAESTHESIA

A SAFE METHOD OF REDUCING OPERATIVE BLEEDING

BY

JOHN BULLOUGH, M.B., B.S., M.R.C.S., D.A.

Visiting Anaesthetist to Ormskirk County Hospital and Southport General Infirmary

Anaesthetists are interesting themselves in the reduction of operative bleeding. One of numerous possible angles from which to attempt this—the lowering of the patient's arterial blood pressure—has received attention recently. To what extent this procedure may safely be applied remains to be seen. The object of this article is to draw the attention of anaesthetists to a simple technique of inhalational anaesthesia which, among other advantages, safely reduces operative bleeding, and, coupled with the intelligent use of posturing the patient, makes the use of drugs to lower the arterial blood pressure unnecessary on most occasions, since such bleeding as does occur is insufficient materially to influence the surgeon's operating conditions.

The technique described is a development of the T-piece technique of Ayre (1937a, 1937b), which was intended, among other things, to reduce vascular congestion during operative surgery. My technique differs from Ayre's in several respects: no additional apparatus is required, endotracheal intubation is unnecessary but may be used, nitrous oxide is the main agent used, air is excluded from the inhaled mixture, only minimal quantities of the volatile agents are used, a change to a semi-closed circuit can be accomplished in a matter of seconds, and the passage of gases through the "T" is different.

Ayre's Technique

Ayre's T-piece technique is briefly as follows. The apparatus consists of a series of tubes for the passage of gases connected together by a small T-shaped metal junction. A small flow of oxygen (2 litres a minute) carrying a high concentration of ether vapour is passed from an anaesthetic machine along some narrow-bore tubing through the vertical limb of the T junction into the horizontal limb (see Fig. 1). The proximal part of the horizontal limb is connected to an endotracheal tube through which gases enter the patient's lungs; the distal part is connected to a short length of wide-bore tubing which is open to the atmosphere. This part of the apparatus forms a small reservoir for oxygen, ether vapour, and gases from the last expiration. The degree of rebreathing can be controlled by varying the length of this distal piece of tubing. Thus expiratory valves and rebreathing-bags are dispensed with; the patient breathes oxygen, ether vapour, and air, at atmospheric pressure, with negligible resistance to inspiration or expiration. Resistance to expiration is a potent source of vascular congestion, and thus of increased operative bleeding. The only other available methods of inhalational anaesthesia which eliminate resistance to breathing are true "open-mask" techniques and insufflation techniques, both of which have distinct disadvantages which make them inferior to the T-piece technique.

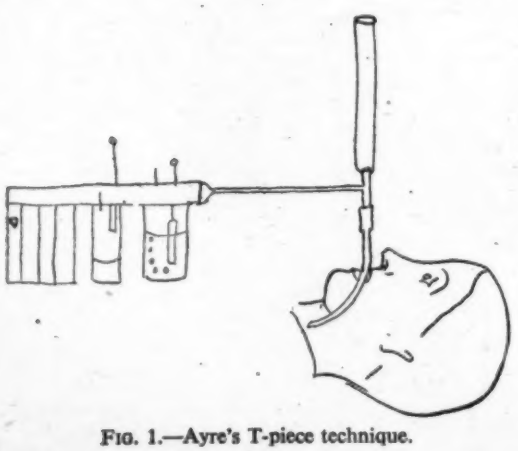


FIG. 1.—Ayre's T-piece technique.

Ayre's technique is probably unsurpassed as a method of inhalational anaesthesia for operations on small children about the head and neck; it has, however, a number of disadvantages which may account for its being seldom used for other types of operations. The disadvantages are: (1) Additional apparatus is required. (2) Some anaesthetists find that fitting the apparatus together is tedious. (3) Endotracheal intubation is necessary, and may not be justifiable for a minor type of operation. (4) A change to other techniques cannot readily be made. (5) Artificial respiration by inflation of the lungs cannot readily be achieved. As relaxant drugs are so commonly used, a means of inflating the lungs is often necessary. (6) Relatively large quantities of ether are required to maintain anaesthesia, as the vehicle is a mixture of air and oxygen. (7) There is an explosion hazard.

The following technique overcomes all these disadvantages and enables the T-piece principle to be used for any type of operation and any type of patient.

Modified Technique

The T in this technique consists of two large-bore lengths of corrugated tubing connected together by a large-bore metal T junction (on which is mounted an expiratory valve), as supplied as standard apparatus for any circle-type absorption unit. At the distal ends of

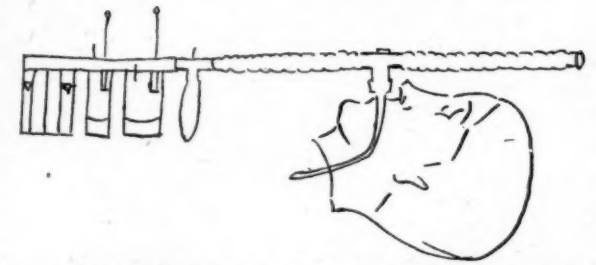


FIG. 2.—Modified T-piece technique, using endotracheal tube. The corrugated rubber tubing is shown as about one-third its correct length.

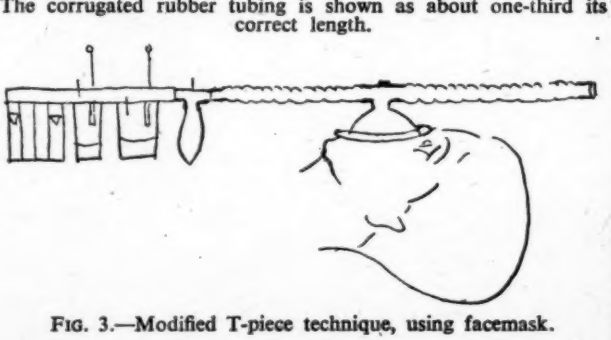


FIG. 3.—Modified T-piece technique, using facemask.

the rubber tubing are metal connexion-tubes. A mask, or endotracheal adaptor, is connected in the usual place. A high flow of fresh gases, 8 litres a minute, is passed through the apparatus; it consists of 75% (6 litres) nitrous oxide and 25% (2 litres) oxygen, with the vapours of any volatile anaesthetic agents as required (see Figs. 2 and 3). The two lengths of corrugated tubing form the horizontal limb of the T in this technique, and the patient takes gases from it via the vertical limb, which consists only of the facepiece mount; the passage of gases is thus somewhat different from that obtaining in Ayre's technique.

In practice, Boyle's apparatus is used as follows. The single corrugated tubing is detached from the usual semi-closed unit (Magill unit) at the junction just distal to the reservoir bag, and in its place, at this point, one end of the double-hosing unit is plugged in. A facepiece is attached in the usual place, and the other end of the double-hosing unit is left open to the atmosphere. The apparatus is now ready for use.

Boyle's apparatus fitted with a Coxeter–Mushin absorption unit can be used as above, or in a simpler way. The Coxeter–Mushin unit is in use, shall we say, as a semi-closed circuit, the soda-lime is turned off, the rebreathing dial is set at 50%, and 6 litres of nitrous oxide and 2 litres of oxygen are flowing, the anaesthetic being administered through either a facemask or an endotracheal tube. Now, if the hosing on the expiratory side is disconnected from the absorption unit and the open expiratory port plugged with gauze or a cork, the T-piece principle is in action. It is not necessary to alter the rebreathing control, as rebreathing cannot take place into the reservoir bag on account of a gravity valve on the inspiratory side. This valve is kept open by the high flow of fresh gases, and thus does not form any obstruction to inspiration in this technique. A small amount of fresh gases tends to accumulate in the bag, which is a desirable thing.

A Marrett apparatus can be converted in the same way, and a metal stopper is supplied with the apparatus for insertion into the expiratory port, though it is supplied for another reason. When the Coxeter–Mushin or Marrett apparatus is in use a change to conventional circuits is made by reversing the procedure, which takes only a few seconds. When Boyle's apparatus is in use a change to a semi-closed circuit is very simply made, by covering the open end of the hosing with the hand, the expiratory valve on the T junction being partly open. In either case manual inflation of the lungs is readily achieved.

By this technique air is prevented from entering the patient's lungs by the high rate of flow of fresh gases and the large volume of gases in the apparatus, which exceed the patient's minute-respiratory volume and his tidal exchange respectively, as the physics of the matter will show.

Physics

The volume of gas contained in the double rubber hosing unit is about 600 ml.—300 ml. on each side of the T junction. Let us suppose that the patient is breathing fifteen times a minute, and that his tidal volume (exchange) is 500 ml., a common occurrence when this technique is in use. His minute-respiratory volume is 7,500 ml. With a flow of 8 litres of fresh gases a minute, the patient's minute-respiratory volume is exceeded, and so no carbon dioxide can accumulate in the apparatus except under the facemask. This can be ignored except when the patient is a very small child or when the tidal exchange is greatly reduced.

A flow of 8 litres of fresh gases a minute equals 133 ml. a second, or 532 ml. in four seconds. With a respiratory rate of fifteen a minute, the patient inspires once every four seconds. During these four seconds 532 ml. of fresh gases have entered the apparatus, and so the patient inhales 250 ml. of fresh gases from the inspiratory side of the rubber hosing from the reservoir bag, and 250 ml. of gases from the expiratory side of the rubber hosing, consisting partly of fresh gases and gases from his last expiration. In order to draw air into his lungs the patient will need to take a considerably deeper breath, for there is the dead space under the facemask, about 50–100 ml., and his own anatomical dead space, 150 ml., intervening between his lungs and the atmosphere. If, however, there is no reservoir bag on the inspiratory side of the apparatus the patient will take about 100 ml. of fresh gases direct from the flowmeters, 300 ml. of gases from the expiratory side of the hosing, and the remainder of his inhalation will be air. This would be a similar state of affairs to that in Ayre's technique.

A measure to prevent the entry of air into the lungs in this event, or if the patient is breathing too deeply, is to attach a further length of hosing to the expiratory side, in the shape of the single rubber hosing from the Magill unit which may be lying idle. It is important not to allow any air to enter the patient's lungs, otherwise the potency of the inhaled mixture is considerably weakened, as it is mainly nitrous oxide that is maintaining anaesthesia in this technique.

Clinical Application

In practice it is advisable to get the patient well settled by another technique before applying the T-piece principle, so that breathing is quiet and regular. For an adult intravenous thiopentone is excellent; for a small child an open-mask technique may be used. If an open-mask or semi-closed technique is used for the induction a quietening in the patient's breathing accompanied by a reduction in the amount of operative bleeding will usually follow the change over to the T-piece technique.

As an illustration of the technique, this would be the anaesthetic procedure for an operation such as a mastectomy. Premedication need only be light, with the customary doses of morphine and atropine, or "omnopon" and scopolamine. Induction takes place in the anaesthetic room with intravenous thiopentone, 0.25–0.5 g. being used as required; the syringe is left in place or a Gordh attachment is fitted to the needle. The patient is now transferred to the operating table. To get the patient settled further intermittent injections of thiopentone are given until he has received, say, 0.75–1 g. This will produce about ten minutes of surgical anaesthesia and a basal level of narcosis for about an hour in an average patient. During this initial period of ten minutes the patient will have been placed in position for operation, the diathermy pad applied, the skin prepared, the towels fixed, and the inhalational anaesthetic and operation started.

The facemask is applied as soon as convenient, with 6 litres of nitrous oxide and 2 litres of oxygen running. This concentration of nitrous oxide may be sufficient to maintain a very light plane of anaesthesia in some patients following the drugs previously given, but other agents will usually be required to prevent reflex response

to operative stimuli, such as movements of the limbs or face, laryngeal activity, respiratory changes, rise in pulse rate, and other phenomena. Any desired supplement may be used, according to the preference of the anaesthetist, such as low concentrations of trichlorethylene ("trilene"), "vinesthene," ether, or even cyclopropane (100–200 ml.); alternatively, further intermittent injections of thiopentone or injections of pethidine may be given. If trichlorethylene or ether is used it is only necessary to raise the lever of the Boyle's bottle to the top of the second division, plunger up. Changes in cardiac or respiratory rhythm are extremely rare when trichlorethylene is used, and this is probably the most useful supplement, as it is non-explosive and has a very potent analgesic action.

Should the patient's tidal exchange become inadequate for his metabolic requirements some degree of cyanosis will usually follow if his blood haemoglobin is normal, since the concentration of oxygen in the inhaled mixture approximates to that of atmospheric air : this is a safeguard against carbon dioxide accumulation in the patient which may follow shallow breathing—another common cause of increased operative bleeding. Cyanosis may be remedied by one of several methods : by increasing the rate of flow of oxygen or decreasing the rate of flow of the nitrous oxide, by adding 500 ml. of carbon dioxide to the flow of gases, by changing to a semi-closed circuit, and by assisting respiration by bag-pressure. These measures should not, however, be prolonged, as they will detract from the benefits of the technique, particularly as regards the quantity of operative bleeding.

Should the patient's breathing become too deep there will be a danger that air may enter his lungs, which will in turn be followed by a rapid lightening of anaesthesia, so that immediate action is called for. An injection of thiopentone will usually have the desired effect, but if this is not possible the flow of nitrous oxide should be raised temporarily to 8 litres, the concentration of supplementary agent increased, or perhaps an injection of pethidine made. If the depth of breathing is not soon decreased it is advisable to change to a semi-closed circuit until the patient comes under control, lest he should return to consciousness. The addition of a second length of rubber hosing to the expiratory side of the apparatus will also help to prevent entry of air into the lungs.

A rather useful point about this technique is that, by the simple expedient of applying the open end of the rubber hosing to his ear, the anaesthetist is able to listen to every breath that the patient takes ; thus positive proof is continuously available that the patient is breathing adequately through a clear airway, or otherwise, as the case may be. This should be very useful during intracranial operations.

The technique has the disadvantage that comparatively large quantities of gases are used ; but then these are very cheap compared with intravenous drugs. There is also the inconvenience of changing cylinders. Body heat and water vapour are lost by the patient to the atmosphere; but this loss is a totally normal occurrence, and is no greater than in normal breathing, and can scarcely be said to be harmful.

In addition to the advantages already mentioned, this technique makes the use of nitrous oxide and oxygen, with truly minimal quantities of supplementary agents, a practical proposition when the patient is a small child, and it has been safely and satisfactorily used on patients as young as 1 year old. This is perhaps because there is the minimum of interference with normal physiological breathing. In this respect the technique compares favourably with open-mask techniques, and is recommended to those anaesthetists whose surgical colleagues insist on the use of "open ether" for such operations as thyroidectomy.

Summary

The use of the T-piece principle of inhalational anaesthesia is offered as a safe and satisfactory method of reducing operative bleeding.

Ayre's T-piece technique is briefly described and its disadvantages are mentioned.

A technique which overcomes these disadvantages is described.

An account is given of two simple ways of converting standard apparatus to the T-piece principle. No additional apparatus is necessary, but endotracheal intubation may be used. Nitrous oxide is the main agent ; air can be excluded from the inhaled mixture. A change to or from a semi-closed technique can be accomplished rapidly.

The technique may be used for adults or children, and for any type of surgical operation.

The applied physics of the technique is outlined.

As an illustration, a typical anaesthetic for a patient undergoing a mastectomy is described.

REFERENCES

Ayre, P. (1937a). *Lancet*, **1**, 561.
—— (1937b). *Anesth. & Analg.*, **16**, 330.

Medical Memorandum

Leukaemia With Primary Gynaecological Manifestations

Although leukaemia in association with pregnancy has been reported and discussed in many recent papers, a search of the *Quarterly Cumulative Index Medicus* shows no report in recent years dealing with leukaemia from the gynaecological aspect. Therefore the admission to one hospital of three such cases as acute gynaecological emergencies in a short period appears to be worthy of record.

Case 1

An unmarried woman aged 22 was admitted on April 17, 1947, at her doctor's request as a case of pneumonitis complicated by abortion. She stated that she had had a cough all her life, that it had been worse for the past month, with pain in the right side of the chest, night sweats, but no sputum. Menstruation had always been normal and regular, but she had bled severely from the uterus for seven days preceding admission to hospital.

She was pale, weak, and very ill. Her blood pressure was 130/60. A faint macular eruption was present on both legs, from the thighs to the ankles. There were signs of consolidation at the right base of the lungs, and the tip of the spleen was just palpable. On rectal examination the cervix and uterus appeared to be normal. An immediate blood count was as follows: red cells, 2,350,000 per c.mm. ; Hb, 40% ; C.I., 0.79 ; blood group, A ; white cells, 1,075 per c.mm. (polymorphs 33%, lymphocytes 64%, monocytes 3%) ; platelets very scanty ; nucleated red cells, 25 per 100 white cells ; bleeding time 10 minutes (normal by method used 1–2 minutes). A film of sternal marrow was reported as showing "great reduction in white blood cells ; only a few polymorphs and myelocytes seen in many fields. There are a fair number of nucleated red cells of rather early

type." *X*-ray films of the chest showed "consolidation of lower portion of right upper lobe." Sputum report: "No tubercle bacilli seen in three specimens." Culture: "*Staphylococcus aureus* and *Micrococcus catarrhalis*."

Repeated blood transfusions caused no change in the blood picture, each transfusion appearing to restart uterine bleeding. On May 26 a complete left-sided facial palsy developed. On June 13 *x*-ray examination showed complete resolution of the consolidation in the right lung. On June 14 the blood picture suddenly changed: red cells, 5,360,000 per c.mm.; Hb, 82%; white cells, 292,000 per c.mm. (neutrophil polymorphs 3%, eosinophils 1%, lymphoblasts 4%, myeloblasts 92%); a few nucleated red cells present; platelets very scanty.

Treatment was started with urethane, but on June 25 there was complete nasal obstruction from oedema and haemorrhage into the nasal mucous membrane, haemorrhages into both conjunctivae and the soft palate, and considerable enlargement of all the groups of glands in the neck. The patient died on July 7. A post-mortem examination was refused.

Case 2

A housewife aged 40 was admitted on September 2, 1948. She was sent to hospital with a letter from her own practitioner which stated: "Please admit. Severe uterine haemorrhage for five months. Confined nine months ago." She was seen by the gynaecological registrar, who reported: "Looks pale, thin, and ill. Abdomen N.A.D.; a few small glands both groins. P.V.: heavy loss. Cervix soft and patulous, feels and looks quite healthy. Uterus soft, bulky, and anteverted. Fornices clear. May be incomplete abortion, or placental polypus, or chorionepithelioma. For diagnostic dilatation and curettage when general condition better."

She was admitted to a ward, where a general examination showed no abnormality, except that the tip of the spleen was just palpable. A blood examination was made and the report was as follows: red cells, 900,000 per c.mm.; Hb, 22%; platelets very scanty; white cells, 8,200 per c.mm. (polymorphs 7%, lymphocytes 37%, myelocytes 3%, myeloblasts 53%). Sternal puncture: myeloblasts, 75%; neutrophil myelocytes, 9%; eosinophil myelocytes, 7%; polymorphs, 5%; eosinophils, 1%; basophil normoblasts, 3%; polychromasic normoblasts, 2%.

Repeated blood transfusion and deep *x*-ray therapy were given. The patient went home at her own request on October 6. She gradually deteriorated and died about three months later.

Case 3

An unmarried woman aged 22 was admitted on April 1, 1949, as a case of "uterine haemorrhage with slight haematemesis." On admission she said that her menstrual period had begun 14 days previously and had continued ever since. She had always bruised easily. One week before the onset of the last period her gums had bled; this was followed by an abscess in the region of the upper left molar teeth which had subsided after penicillin injections. She had started to vomit small flecks of blood-stained material on the morning of the day of admission. Further, she had previously attended two other hospitals for severe dysmenorrhoea with excessive blood loss. One of these hospitals informed us that in March, 1946, her haemoglobin had been 94%, white cells 7,000 per c.mm., with a normal differential count. The other said that in January, 1947, she had had a haemoglobin of 104%.

She was pale, with a marked gingivitis. The lungs, abdomen, and central nervous system showed no abnormality. There was a harsh systolic murmur in all the cardiac areas. A blood examination was made immediately on admission: Hb, 40%; white cells, 28,800 per c.mm. (polymorphs 20%, lymphocytes 12%, metamyelocytes 2%, myelocytes 6%, myeloblasts 60%); nucleated red blood cells, 6 per 100 white blood cells; platelets very scanty. Sternal puncture confirmed the picture of an acute myeloblastic leukaemia.

Repeated blood transfusions and urethane were given, and, although the white-cell count dropped to 8,800 with only 5% myeloblasts, the clinical course was one of steady deterioration, with haemorrhages in the optic fundi and large haemorrhages all over the body. She died five weeks after admission.

At necropsy the spleen was of normal size, the liver large and infiltrated, and the bone marrow everywhere replaced by a soft pink material.

Comment

Most textbooks of haematology and of gynaecology make but brief reference to the possibility of leukaemia as a cause of uterine bleeding. Thus Whitby and Britton (1946) state regarding leukaemia, "Multiple haemorrhages in the retina, ear, spinal cord and brain, or from the uterus, kidney, or bowel, may all be found," but state, further, that "in myelocytic leukaemia, amenorrhoea or scanty menstruation is common." Moore White (1944) says: "Uterine haemorrhage may be a symptom of most of the blood diseases." Browne (1950) comments more fully: "Such blood diseases as splenic anaemia, idiopathic hypochromic anaemia, aplastic anaemia, leukaemias, and thrombocytopenic purpuras may be associated with menorrhagia. Secondary thrombocytopenia arising from malignant neoplasms, leukaemia, septicaemia, arsenical poisoning, and *x*-ray or radium therapy may so depress that bleeding time is prolonged and menorrhagia may occur." It is to be noted that in all three cases described the platelets were very scanty. Several other standard textbooks consulted make no reference to the possibility of uterine haemorrhage being caused by leukaemia.

This hospital, being one of the former municipal hospitals of London, has always received large numbers of cases of uterine haemorrhage, the greater number of which prove to be due to abortions; in fact, 550 cases of abortion were admitted during the period covered by the three cases described. The occurrence of cases such as these points to the urgent need for a full blood examination in all cases of uterine haemorrhage, before the almost inevitable dilatation and curettage operation is performed, particularly when the patient is exsanguinated or when there is any haemorrhage into the skin or from any other unexpected site. In such cases the operation cannot be expected to be of any benefit to the patient, but would only be an additional and major discomfort in the course of a most distressing illness.

C. E. W. WHEATON, M.D., M.R.C.P.,
Physician, Lambeth Hospital.

REFERENCES

Browne, F. J. (1950). *Post-Graduate Obstetrics and Gynaecology*, p. 260. London.
Whitby, L. E. H., and Britton, C. J. C. (1946). *Disorders of the Blood*, 5th ed., pp. 416, 422. London.
White, M. Moore (1944). *The Symptomatic Diagnosis and Treatment of Gynaecological Disorders*, p. 57. London.

The 1951 *Register* of Chiropodists has just been published by the Board of Registration of Medical Auxiliaries listing the names, addresses, and qualifications of chiropodists recommended by the Board to the medical profession, hospitals, education authorities, etc. It is available free to members of the medical profession, hospitals, and official bodies; application should be made to the Registrar, Board of Registration of Medical Auxiliaries, B.M.A. House, Tavistock Square, W.C.1.

Reviews

THE BEGINNING OF LIFE

The Physical Basis of Life. By J. D. Bernal, F.R.S. (Pp. 80. 6s.) London: Routledge and Kegan Paul. 1951.

When Wöhler in 1828 showed that urea can be made from laboratory chemicals he broke down one of the high walls between the worlds of living and dead matter. More recently the discovery that some viruses can lie dormant as crystals for years, and then come to life on their host, seemed to break down another wall. But no such wall is ever the last; and to this day no scientist can sustain with experiments his private conviction that the organic molecules have grown from the inorganic molecules by natural and intelligible steps.

Professor Bernal is not a man to shirk his convictions, and in this small but fundamental book he has not been content with any makeshift answers. In what conditions could large protein-like molecules have grown? he asks. How did they reach the asymmetry which characterizes living molecules? And what was it about their structure which made them capable of copying themselves in the living process? Finally, why do the early conditions no longer hold to produce new life spontaneously to-day?

Professor Bernal answers by tracing the probable history of the sea and the air when first the earth cooled. The sea water would first contain ammonia, carbon dioxide, and hydrogen sulphide; the air would contain no oxygen, and therefore no curtain against the most penetrating ultra-violet light. Under its action, it is reasonable to think that some simple amino-acids would then be formed.

But now comes the crucial question: How would these be concentrated and built up into the first protein-like molecules? The essential property which Professor Bernal uses for this step is the catalytic action of clay in shaping molecules which grow in contact with it. This is commercial practice in the oil industry to-day, but it has not been proposed before as the foundation of a scientific theory of life. Clay alone would not grow asymmetric molecules; but quartz would; and in either case the resulting primitive protein might well have a structure stable enough to shape and copy other molecules by catalysis—that is, to become a primitive enzyme.

As for repeating the experiment, Nature can no longer do so, because plants have since filled the air with shielding oxygen. Moreover, the very growth of life has of course destroyed the aseptic conditions in which life began. It remains for Professor Bernal to improve on Nature and repeat the experiments in the laboratory.

This will not be the last book written on this subject. But it is a book of wide and vigorous learning which never compromises with its own uncertainties. Neither Professor Bernal nor the reader is meant to suppose that he has indeed hit precisely upon the very process, step by step, which Nature used to make life. But he has, I hope, killed once for all those idle speculations which look for life in the chance encounter of atoms and then learnedly compute the odds against it. Life was not created by accident; it grew continuously from its own probabilities; and Professor Bernal has made it plain that they are inherent in its simplest atoms.

J. BRONOWSKI.

BLEULER ON SCHIZOPHRENIA

Dementia Praecox or the Group of Schizophrenias. By E. Bleuler. Translated by Joseph Zinkin, M.D. Foreword by Nolan D. C. Lewis, M.D. Monograph Series on Schizophrenia No. 1. (Pp. 548. £3 3s.) London: Methuen and Co. 1951.

It would be an interesting exercise to consider what the effects on Anglo-Saxon psychiatry might have been had this classical monograph been translated from the German shortly after its first appearance in 1911. Certain it is that much of the confusion and controversy over the concept of schizophrenia—the name dates from Bleuler's book—would never have arisen if British and American psychiatrists had had earlier access to this clear exposition. It is true that excerpts have been incorporated in our popular English textbooks, so that the salient features of Bleuler's conception are familiar to all. But for many readers this translation will give the first opportunity to observe how a searching and creative mind took a mass of carefully collected clinical observations and out of these welded a comprehensive theory of the disease which has largely stood the test of time. The achievement is all the more remarkable when we recall that it took place in an era when Continental psychiatrists had not emerged from the necessary but comparatively limited "classificatory" phase.

Bleuler's restricted and cautious application of Freudian psychology to the major psychoses, his unorthodox and courageous approach to practical problems of treatment, and his penetrating and independent power of observation have made him one of the most influential personalities in twentieth-century psychiatry. All these facets of the true scientist are to be seen in this book, and here for the first time he distinguishes between primary and secondary psychological symptoms—that is, between those specific symptoms caused by the basic disease process and those accretions which are the reaction of the mind to the primary changes. Although Bleuler's application of this principle to schizophrenia has dated—as naturally many other of his ideas have dated with the passage of time—the principle itself has found wide recognition and from it has grown the "pluridimensional approach" (of Kretschmer and Birnbaum) to psychiatric symptomatology and diagnosis. Bleuler's concept of a hierarchy of symptoms—specific, constitutional, reactive, accidental, etc.—has proved far superior to the uniform sequence of "reaction types" which was conceived about the same time by Adolph Meyer. Dr. Zinkin has made a faithful rendering of Bleuler's thought and couched it in easily readable English.

W. MAYER-GROSS.

COELIAC DISEASE

Management of Celiac Disease. By Sidney Valentine Haas, M.D., and Merrill Patterson Haas, M.D. (Pp. 188; 12 illustrations. £2.) Philadelphia and London: J.B. Lippincott Company. 1951.

It is a misfortune that this book should have appeared just at a time when, thanks to the work of Dicke and others in Holland and Sheldon in London, the exact part played in this malady by carbohydrates is becoming clearer. The distinction which can now be made between the effects of wheat flour and those of wheat starch must surely lead to some modification of the Haas hypothesis, which condemns all polysaccharides. This hypothesis pervades the whole book and detracts

inevitably from its value, but students of the subject will be grateful for the history of coeliac disease, for the full discussion of clinical symptoms, and for a most useful bibliography. (It is again a minor piece of bad luck that in quoting a small contribution to the subject by the reviewer the authors have spelt his name wrongly and repeated this error in the bibliography.)

Experience gained over many years of treating hundreds of patients gives the authors much to discuss, but it has perhaps also blinded them to the value of the work of others. Coeliac disease to-day can be cured without the bananas which Professor Haas pioneered. Few would accept (pp. 123–4) that, "if cystic fibrosis of the pancreas is treated by the same dietary regimen that is used in celiac disease, the diarrhea will cease, nutrition will become normal, and if the pulmonary infiltration has not become too severe, it too will clear up." After this it is not surprising to find that the authors make light of the diagnostic value of estimating the trypsin in duodenal juice. The authors' final summarized hypothesis reads as follows: "The diarrhea of celiac disease is caused by an anthroquinone irritant produced by a micro-organism from a polysaccharide substrate." Various paths of investigation to test this hypothesis are outlined.

ALAN MONCRIEFF.

U.S. PUBLIC HEALTH SERVICES

Medical Care of Seamen. The Origin of Public Medical Service in the United States. By Robert Straus. With preface by Leonard A. Scheele, Surgeon General, Public Health Service. (Pp. 166. £1 4s.) Merchant Seaman Studies, Volume 1. New Haven: Yale University Press. London: Geoffrey Cumberlege (Oxford University Press). 1950.

The title of this book is misleadingly restricted, for the author defines the conditions under which the U.S. Federal Government has entered the field of medical services, and he traces certain trends which in his view indicate the future development of a general medical service. He shows how the Federal services have evolved through expansion and amalgamation of schemes started to meet new needs. The process is illustrated by the history of the Public Health Service, which has grown out of the Marine Hospital Service, founded in 1798 on a contributory basis.

American merchant seamen appear to have been less socially integrated than those of other countries, who came within the framework of the general public medical provision. This factor, together with the concentration of the population on the Atlantic coast, the many inland waterways crossing state boundaries, and the boarding-house racket, created a problem peculiar to the U.S.A., and one which only the Federal Government could solve. Dr. Straus summarizes the developments made in the service and the contributions from welfare agencies, unions, and ship-owners; in tabular form he compares these with the services in other countries. He shows how in 1884 the service ceased to be contributory and how it became responsible for certain preventive measures protecting the whole nation, so that in 1912 its title was changed to the Public Health Service. Dr. Straus discusses the impetus which it received from two world wars and from the Social Security Act of 1935, and brings its history up to date with brief references to its growing responsibilities and authority. The early emphasis on preventive measures is remarkable, and quotations reveal a strong social medical approach as early as 1873.

This brief study is presented in a pleasant and clear style, but the weighty reading on which it rests is apparent in the references. The author is incorrect in stating that the Marine Hospital Service had a precedent in the United Kingdom. The mistake is due to his believing that the Chatham Chest and Greenwich Hospital made provision for merchant seamen as well as for naval ratings. He has high authority for his error, since it was apparently made in Congress in 1884. It would, however, be ungenerous to dwell on this minor point in a book which so completely fulfils its purpose and which provides English readers with much information about American public medical services, previously available to them only from scattered and obscure sources.

J. J. KEEVIL.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Human Anatomy and Physiology. By N. D. Millard, R.N., M.A., and B. G. King, Ph.D. 3rd ed. (Pp. 596. 22s.) London: W. B. Saunders. 1951.

Science News 21. Edited by A. W. Haslett. (Pp. 126. 2s.) Harmondsworth: Penguin Books. 1951.

Handbook of Experimental Psychology. Edited by Professor S. S. Stevens. (Pp. 1,436. 120s.) London: Chapman and Hall. 1951.

The British Encyclopaedia of Medical Practice. Edited by Lord Horder, G.C.V.O., M.D., F.R.C.P. 2nd ed. Vol. 6: Gastritis to Hypermetropia. (Pp. 712. 60s.) London: Butterworth. 1951.

Microbiology for Nurses. By M. E. Morse, M.D., and others. 8th ed. (Pp. 540. 20s.) London: W. B. Saunders. 1951.

Estado Actual de la Terapéutica Antimalárica. By Dr. R. V. Ulloa. (Pp. 203. 20 pesetas.) Barcelona: Byp. 1951.

Bevölkerungsdynamik und Bevölkerungsbilanz. By Professor F. Burgdörfer. (Pp. 116. M. 8.) Munich: J. F. Lehmanns. 1951.

Die Narkoanalyse als initiale Methode in der Psychotherapie. By Professor C. Fervers. (Pp. 120. M. 7.50.) Munich: J. F. Lehmanns. 1951.

Die Lungentuberkulose im Röntgenbild. By Dr. W. Hirsch and Dr. H. Liebau. (Pp. 142. M. 20.) Leipzig: Georg Thieme. 1951.

Atlas der Pathologischen Anatomie. By Dr. R. Rössle and Dr. A. Apitz. (Pp. 298. M. 87.) Stuttgart: Georg Thieme. 1951.

Wissenschaftstheoretische Aufsätze für Ärzte. By Professor G. Ricker. 2nd ed. (Pp. 82. M. 5.70.) Stuttgart: Georg Thieme 1951.

Das Verstehen und Begreifen in der Psychiatrie. By Professor F. A. Kehrer. (Pp. 58. M. 5.70.) Stuttgart: Georg Thieme. 1951.

Bionome Psychotherapie. By Professor J. H. Schultz. (Pp. 186. M. 11.70.) Stuttgart: Georg Thieme. 1951.

Die Intravenöse Anwendung der Lokalanästhetika in der Inneren Medizin. By Dr. G. K. Kraucher. (Pp. 116. 13s.) Vienna: Springer. 1951.

Arzneitherapie der Herzkrankheiten. By Dr. H.-J. Oettel. (Pp. 253. M. 27.) Stuttgart: Georg Thieme. 1951.

Fizyopatoloji. By Professor S. Tavat. (Pp. 775. No price.) Istanbul: Mazlum-Kitabevi. 1949.

Pratikte iç Hastaliklari. By Professor R. P. McCombs, B.S., M.D., F.A.C.P. (Pp. 733. No price.) Istanbul: Mazlum-Kitabevi. 1949.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY JANUARY 5 1952

LUNG RESECTION FOR PULMONARY TUBERCULOSIS

The common-sense concept of the radical treatment of pulmonary tuberculosis by removing the offending organ has been attractive for many years, and sporadic attempts to execute it have been made since towards the end of the nineteenth century. Successes were exceptional until the last few years, but to-day excision is the treatment of choice for many types of tuberculosis of the lung: perhaps it will soon be accepted—in practice, as in theory—for all cases of localized disease which will not heal on their own. The results of other longer-established methods of treatment certainly allow no complacency, for, although often highly successful in individuals, considered as a whole they are far from reassuring. Snell[1] has recently reviewed 2,472 cases with positive sputum admitted to Colindale Sanatorium from 1938 to 1950; in only 27.8% did the sputum become negative. The patients in this series were to some extent selected, and the criteria of conversion strict, but these figures are not exceptional.

Fifteen years ago resections were seldom done, because fatalities, complications, and failures were so common. The different results to-day are due, first, to the advances in knowledge of pulmonary surgery and, secondly, to the use of antibiotics, particularly streptomycin. The indications for resection remain to some extent controversial. It is accepted as sound treatment for patients in whom collapse therapy—such as thoracoplasty—has failed, or is likely to fail, because of lower-lobe disease, solid foci or tuberculomas, tuberculous bronchiectasis, or severe bronchial stenosis. It is often done for giant cavities or extensively destroyed lungs or lobes. For children or adolescents who need surgical treatment resection is usually preferable, since loss of lung tissue is well compensated, whereas thoracoplasty leads to severe deformity. Resection may be done when the diagnosis is in doubt before operation and neoplasm is suspected, and sometimes for severe haemoptysis. It can be combined with excision of an overlying empyema if an extrapleural dissection is performed, as Sarot described.[2] Some surgeons, such as Bickford and his colleagues[3] in Liverpool, have extended the indications to include cases of localized disease in which thoracoplasty would have been expected to succeed. For small lesions an excision will often result in less loss of function than would effective collapse treatment. Among the contraindications to resection are extensive active disease outside the area to be resected; poor function of the remaining lung tissue from any cause; active endobronchial disease at the proposed site of division of the bronchus; and infection with organisms insensitive to streptomycin. Whereas collapse operations are seldom indicated except in patients with a high general resistance and stable radiographic findings, an excision may succeed in a toxic patient, occasionally even in one desperately ill with high fever and copious sputum.

Pulmonary tuberculosis is very commonly a bilateral disease, and often more widespread than radiographs suggest. By resection only the major lesion is removed. Small areas of disease are usually left behind; these remain or become healed in the same way as does the bladder after removal of a tuberculous kidney. The extent of resection necessary is indicated by preoperative radiographs. If contralateral disease is present it should be controlled by artificial pneumothorax or have shown no signs of spread for at least 12 months. Whether pneumonectomy or lobectomy is performed will depend on the distribution of the disease, but when it is localized segmental resection is often indicated, as advocated by Chamberlain.[4] In such cases tomography, particularly in the lateral plane, should be carried out to exclude active foci in the residual tissue, and the findings confirmed by palpation at the time of operation. Local excision or enucleation of a small focus may perhaps be the ideal treatment for a contralateral lesion or for a solitary tuberculoma, but its place is not established. As microscopic tubercles are often present in apparently normal lung adjacent to the diseased area a fairly generous margin should be left; if the intersegmental or interlobar plane is obliterated a little of the adjacent normal segment can be included with the resection.

Details of operative technique vary a little in different surgeons' hands. The patient is often put into the prone position, since it allows secretions to drain into the trachea during the operation. The extrapleural approach to the hilum may make dissection easier and is said to leave the tissues less liable to secondary infection. Reinforcement of the sutured bronchus by a pleural or muscular flap may reduce the incidence of imperfect healing. Streptomycin,

1 *Lancet*, 1951, **2**, 415.
2 *Thorax*, 1949, **4**, 173.
3 Ibid., 1951, **6**, 25.
4 *J. thorac. Surg.*, 1950, **20**, 843.
5 *British Medical Journal*, 1951, **2**, 839.
6 *Thorax*, 1951, **6**, 230.
7 Ibid., 1951, **6**, 369.
8 *J. thorac. Surg.*, 1950, **20**, 854.

with P.A.S., effectively reduces the incidence of complications and of post-operative spread of disease, and should always be given as a cover for operation. Most surgeons advise a period of three to six months' rest in bed under sanatorium conditions after the operation; the principal reason for this is to ensure healing of the residual disease. Perhaps it will later be found that in strictly localized lesions this can be dispensed with. It is hoped and expected that one of the advantages of resection as a method of therapy is that it will markedly shorten the total period of treatment. Surgeons have not yet discovered the best way of dealing with the dead space left after resection. As there are so often small healed areas of disease in the remaining lung, its overstretching by compensatory emphysema should be avoided, since this might cause a flare-up. Sometimes, especially after pneumonectomy, foreign bodies such as plastic spheres have been left in the space,[5] but more often it is closed by thoracoplasty. This may be combined with division or crush of the phrenic nerve and pneumoperitoneum, which is best induced before the operation. After lobectomy the thoracoplasty may be less extensive, or unnecessary, and in most cases of segmental resection the space is small and no special measures are needed to close it. Thoracoplasty is usually done two or more weeks after the resection, but recently it has been shown that it can be performed at the same time, as described by Waddington,[6] and by Cruickshank and El Papamichael,[7] without appreciably increasing the risk.

Serious complications of lung resection for pulmonary tuberculosis are bronchial fistula and empyema, which often occur together and may be due to tuberculous or to secondary infection. Spread or reactivation of disease is less common. No series of patients have yet been followed for very long. Bickford and his colleagues have reported on nearly 100 cases, observed for a year or longer: two of the patients died while under observation, but a positive sputum had become negative in 87% of the survivors. Day and his colleagues[8] treated 202 patients by resection; 25 died, but of the remainder 85% had negative sputum. Similar figures have been reported by other American authors.

HOUSE DUST AS AN ALLERGEN

It is surprising that more effort is not being devoted to the study of allergy, for according to one authority "allergic diseases, with a prevalence of 1,337 per 100,000 population, are commoner than gastric, duodenal, peptic, and anastomotic ulcers combined, than all forms of anaemia, between three and four times as common as angina and valvular heart disease combined, and rheumatoid arthritis, osteoarthritis, and spondylitis combined."[1] Unfortunately the techniques used by earlier investigators were qualitative only, and the initial enthusiasm surrounding the discovery of so striking a phenomenon led during the immediately succeeding years to much uncritical work and earned for the subject a certain degree of disrepute in this country. Despite the unpopularity of allergy as a subject of investigation, certain outstanding investigators have during the last two or three decades added greatly to our knowledge of the fundamental principles governing allergic responses. A new era seems now to be dawning in this field of research, owing largely to the application of the techniques of microchemistry and biophysics, which render possible investigations upon a quantitative basis.[2] The importance of the working hypothesis in the advancement of medical science still remains, as Professor J. R. Squire ably demonstrates in the paper published in the opening pages of this issue, but the validity or otherwise of hypotheses in the realm of allergy can be more readily tested when a quantitative approach can be made.

It appears evident at once that there is no satisfactory method for the standardization of the commonly occurring allergens (such as pollens, dander, or dusts), since there is no relation between potency as tested on the patient and either weight or content of total nitrogen or protein nitrogen. The present stage of development is similar to that reached in the early days of vitamin research, and the only possible recourse seems to be to an arbitrary standard preparation of the material in question, but with the added difficulty that the human subject should really be used for comparison—though multiple sensitivity is just as likely to occur in such a subject as did multiple deficiencies in the animals used for vitamin assay. There is still a great need for further purification and characterization of the known common allergens.

House dust is one of the commoner causes of specific sensitization, estimates of its incidence in asthmatics having varied between 33 and 79%.[3] Assessment of the exact incidence of hypersensitization is made difficult by the possible occurrence of weak positive reactions due either to low-grade sensitivity in patients without clinical symptoms or to non-specific irritant material. By its very nature house dust might be expected to contain a great

1 Williams, D. A., *1st International Congress of the International Association of Allergists*, Zurich, September 23–29, 1951.
2 Rimington, C., ibid
3 —— in H. A. Abramson's *Somatic and Psychiatric Treatment of Asthma*, 1951, Baltimore.
4 *Brit. J. exp. Path.*, 1947, **28**, 309.
5 Ibid., 1947, **28**, 326.
6 *Ann. intern. Med.*, 1937, **11**, 505.
7 *1st International Congress of the International Association of Allergists*, Zurich, September 23–29, 1951.
8 Ibid.

variety of allergens, yet most investigators have been struck by the rather highly specific character of house-dust sensitivity. Rimington, Stillwell, and Maunsell,[4] by purifying the active material, obtained a product which proved to be a polypeptide-like unit combined with a polysaccharide, or a complex of such chemically similar materials. Biological activity was shown to reside in the nitrogen-containing portion of the molecule, since controlled degradation removed the greater part of the carbohydrate without decrease in potency. Acid hydrolysis liberated several common amino-acids, but the basic and aromatic amino-acids were notably deficient. The purified allergen did not give the usual protein reactions, and it is noteworthy that solutions of it may be boiled without loss of activity. It would appear, like the blood group specific substances, to belong to a class of biochemical materials, so far little investigated, in which amino-acids and carbohydrates are associated in a large complex molecule. From three different moulds (*Caldariomyces fumago, Penicillium roqueforti,* and *P. tardum*) grown in pure culture the same workers[5] obtained products similar in composition to the house-dust allergen and reacting specifically in hypersensitive persons. Further research upon these muco- or glycoprotein-like materials is urgently required.

Three principal hypotheses have been put forward to explain the presence of the specific material in house dust: first, that it is derived from the air-borne spores of common moulds; secondly, that it arises from the disintegration of textile fibres, such as cotton, under physical influences (light, heat, etc.); and, thirdly, that it is formed as a result of the action of micro-organisms upon fibres or furnishing materials and is not present in either separately. A brief examination of these possibilities may be of interest. Much work has been devoted to the identification of moulds inside and outside houses and to the testing of dust-sensitive patients with mould extracts, but little support has been gained for the first hypothesis—there is in general a lack of quantitative relationship between dust and mould sensitivity. Similarly the support for the second hypothesis is but meagre. Extracts of "old" fibres often cause large reactions, but in an experiment by Wagner and Rackemann,[6] in which new kapok was "aged" under sterile conditions, no active material was produced in six months. Subsequent spraying with moulds (themselves incapable of giving positive skin reactions) from old kapok quickly led to the formation in the kapok of typical biologically active material. Such a result supports the third hypothesis. Still further support for this possible origin of the house-dust allergen is afforded by Maunsell's[7] investigations of the situation of the homes (in the London area) of dust-sensitive patients with bronchial asthma or perennial rhinitis. Thirty-eight out of 49 patients lived, at the onset of their disease, in houses within 180 yards from open or underground waterways, as against 17 out of 49 strictly comparable controls. Though many of London's small waterways have for long been enclosed in concrete sewers, the clay in their neighbourhood probably has a higher humidity than elsewhere, because rain water over a large area must still gravitate to the regions occupied by these drains. Moulds probably grow more freely in houses built on such damp ground than in houses further from the watercourses. Harsh[8] has pointed out that the warm, humid coast of California, with its low pollen and fungus counts, constitutes an ideal natural laboratory for the study of the effect of climate in allergy, especially since more than 75% of the adult population has lived previously in drier inland areas. As a result of his observation of patients with respiratory allergic diseases who are sensitive to house dust or pollen he concluded that the effect of a damp climate may not be due to external operation of the climate *per se* but rather to an effect of the humidity in potentiating the allergen.

At this stage it would be well to recall Professor Squire's analysis of the place of hypothesis in the advancement of medical science. The problem of house-dust sensitivity is difficult, and the hypotheses briefly referred to above are provocative; but it will be interesting to see how they bear up under further well-directed experimental assault.

SPECIFIC LANGUAGE DISABILITY

The occurrence of specific language disabilities in children of normal intelligence has long been recognized. Under the rubric of "developmental aphasia" a variety of clinical pictures have been described in which the main feature is "lack of facility in the various aspects of handling words: reading, spelling, talking, and writing." It is rare, however, for all uses of language to be affected equally, and severe retardation in reading or spelling (or both) without any difficulty with speech is quite common. Curiously enough, calculation is seldom affected. The incidence of such defects in the general population has been placed as high as 10%, and there is some reason to believe that they are commoner among boys than girls. The causes and treatment of specific language defects should be more intensively studied, for educational reasons as well as for their relevance to the theory of aphasia. Gallacher,[1] for instance, feels that school medical officers and others concerned with the management of retarded children should give fuller recognition to the

[1] *N. Engl J Med.*, 1950, **242**, 436.
[8] *Acta psychiat., Kbh.*, 1950, Suppl. 65.

existence of developmental language difficulties, and he gives a number of diagnostic features of what he believes to be a specific clinical entity. These include uneven and ill-formed handwriting, slow and stumbling reading (with many mispronunciations and occasional reversals), numerous and bizarre spelling errors, and a bad record in linguistic school subjects. Although suitably cautious about their cause, Gallacher inclines to Orton's well-known theory that such defects result from failure to establish normal hemisphere dominance. But although this hypothesis has proved attractive to many, it has so far failed to establish itself firmly in orthodox neurological theory.

A more extensive study of the dyslexic component (congenital word-blindness) in specific language defect has been reported by Hallgren.[2] Unlike earlier workers, he has been unable to find evidence of a direct association between "developmental dyslexia" and left-handedness, left eye dominance, or mixed eye-hand preferences. These negative findings militate to some extent against the view that anomalous cerebral dominance is a causal factor. On the other hand, Hallgren reports evidence pointing to the congenital origin of the disorder, in a majority of cases at least. Data derived from examination of the parents and siblings of 116 dyslexic children lead him to conclude that the defect follows a "monohybrid autosomal dominant mode of inheritance with practically complete manifestation." If this work be confirmed, it would suggest that specific dyslexia is an inherited defect comparable to colour blindness and that environmental factors play little, if any, part in its causation. The possibility that they may exacerbate a congenital condition is not, however, excluded. The implications of Hallgren's findings for the schooling of children with developmental language defects remain to be assessed. Although some response to remedial methods is often claimed, it appears distinctly doubtful whether this justifies the time and trouble spent on treatment when the defect is certainly congenital. In such cases less attention might be given to the disability itself and more to the development of knowledge and skills in unaffected fields of performance. Such a course, combined where necessary with appropriate psychiatric guidance, might go a long way towards reducing the affected child's sensitivity about his handicap and equipping him for a vocation in which technical skill counts for more than symbolic sophistication.

CHOICE OF ANTIBIOTIC FOR PNEUMONIA

The recent trial[1] published by the Medical Research Council subcommittee showed clearly that penicillin was at least as effective as aureomycin or chloramphenicol in the treatment of bacterial pneumonia—and very much cheaper. In the winter of 1949–50 a group at the Philadelphia General Hospital carried out a similar but smaller-scale trial on a total of 93 patients, and came to much the same conclusion.[2] Indeed, the drop in temperature was most sudden, and secondary rises rarest, in those who received penicillin, even when given orally in a first dose of 500,000 units followed by 250,000 units every 12 hours to a total of 3,000,000 units. End-results were the same with each treatment. Penicillin has the advantage of fewer toxic reactions than the other antibiotics. Because it produces the most rapid response, the authors believe that it is best used even in cases where the pneumonia is not certainly bacterial but may be viral, since it is bacterial pneumonia which has the high mortality.

1 *British Medical Journal*, 1951, **2**, 1316.
2 *J. Amer. med. Ass.*, 1951, **147**, 918.

NUTRITION IN NEW GUINEA

Breadth of knowledge as well as vision is needed in the drawing up of reliable plans for raising the standard of living of the people in the colonial territories.[1] More than one scheme has already come to grief because it was launched without sufficient testing of its suitability. What the planners have apparently failed to realize is that success in a temperate zone gives no guarantee of an equivalent success elsewhere. The report[2] of the New Guinea Nutrition Survey Expedition suggests that the lesson has been well learnt by a group of Australian scientists. Undertaken at the request of the Administrator of Papua and New Guinea and the Department of External Territories, Australia, the expedition's main object was to collect enough information about native dietary patterns and food habits to make possible the drawing up of sound and acceptable ration scales for employed labourers. Secondary aims were the study of normal production and consumption and the collection of data which would help to show whether native agriculture could combine cash and food crops without detriment to the latter.

The field staff consisted of a medical officer, two biochemists, a parasitologist, a nutritionist, an agriculturist, a dental officer, an anthropologist, and a photographer, and they were assisted by various members of the staff of the Institute of Anatomy working in Canberra. The expedition visited five different villages, spending approximately one month in each, and the combined efforts of the different members of the team have provided an all-round review of the situation prevailing at the time of the visit in three of the villages. In the remaining two villages the work was less comprehensive. The people surveyed lived mainly on starchy roots, sago, or bananas, with no milk and practically no flesh food, yet no signs of malnutrition were detected. The weakness of the survey was the short time spent in each village. Experience in other territories has shown how necessary it is to live closely with the people under observation throughout at least one complete agricultural cycle; seasonal fluctuations tend to be much greater than expected, and an understanding of the cultural outlook of an unknown community is not achieved in a short time. The writers of the report seem to have realized this, and most sections end with a call for further investigations. The danger is that readers may be less aware of the many things that were not found

1 *British Medical Journal*, 1951, **2**, 33.
2 *Report of the New Guinea Nutrition Survey Expedition*, 1947, Government Printer, Sydney.

out and too prone to quote figures which may apply only to one month in the twelve. This is not to decry the value of the observations that were made but only to point out that they were extensive rather than intensive. Carefully interpreted, they can be of the greatest use, not only to the territories concerned but also to medical scientists, agriculturists, and others elsewhere.

COMPULSORY RETIREMENT

The age for retirement of doctors in the hospital service has been fixed at 65. Most consultants, knowing that able men have been trained to take their place, have no great objection to this provided they can, if they want to, continue their work in private practice or in other directions. It would in fact be a sad waste of knowledge and experience if all medical men ceased the practice of medicine at the age of 65, or even much higher, and it is disturbing to read recent letters from doctors who have had their contracts with hospitals terminated under the age rule and are left with little or no work to do. Consultants retiring now under this rule have not served in the N.H.S. long enough to qualify for a pension, and their opportunity to make a living out of private practice is much less than it was before 1948. Pathologists and radiologists are particularly hard hit, for many of them did all their work at voluntary hospitals and were paid by salary. The Consulting Pathologists Group Committee of the B.M.A. has recently been considering how to make things easier for those who have to retire under the present rule without a pension (see *Supplement*, page 4). There is in fact a good case for extending the contracts of pathologists beyond retiring age because of the difficulty of finding suitably experienced men to fill consultant posts in this specialty. The clinician is in a far more favourable position, for the granting of an honorary contract to him enables him to continue his work by attending patients in private beds, while an honorary contract is valueless to a pathologist who has no private laboratory of his own, unless he is also given the right to use a hospital laboratory. This might cause difficulties in some laboratories, but with good will and common sense it should be possible to ensure that retired pathologists, and other consultants in like position, can continue to exercise their skill and at the same time overcome the financial hardship caused by the enforced termination of their contracts.

WINTER EPIDEMICS

Lack of knowledge about the differences between the several forms of respiratory disease occurring in epidemics during the winter has delayed the development of specific methods of treatment. But the control of influenza by immunization now seems to be within the bounds of possibility, and the important task of the moment is to obtain information which will not only be of use to laboratory workers but will also help hospitals to meet the strain of a sudden winter epidemic. The person best placed to collect evidence about local outbreaks is the district medical officer of health.

His sources of information, according to a recent suggestion of the Ministry of Health,[1] should be general practitioners, industrial and Service medical officers, the regional controllers of the Ministry of National Insurance, and registrars of deaths. Besides letting the Ministry know as soon as he finds that respiratory disease is becoming unusually prevalent, the M.O.H. must warn the Public Health Laboratory Service at the earliest indication of an outbreak, so that arrangements can be made to collect material for investigation. For this purpose it is hoped that some general practitioners will act as "spotters," who will be in direct touch with the nearest laboratory, though of course the results of tests will probably not be ready in time to help the practitioner in his treatment of an individual patient. By these means the Ministry hopes "that representative strains of virus will be isolated from all the main centres of population at the time of the first appearance of influenza." Meanwhile the Medical Research Council is to study the production and arrange for the trial of a vaccine made from influenza virus cultured in fertile eggs. The hopes that this vaccine may eventually be used with success on a large scale have been recently strengthened by the discovery that its antigenic property is greatly enhanced by the addition of oily adjuvants.

SALMONELLA MINNESOTA INFECTION

The first large outbreak in Britain of food-poisoning caused by *Salmonella minnesota* has occurred in Northamptonshire and the surrounding country, and some information about it is given at page 53. Several hundred people are known to have been affected, and there are thought to have been more whose symptoms were so mild that they did not seek medical attention. There have been two deaths—a woman aged 77 and a man aged 78. The infection has appeared chiefly in the elderly, as is usual in outbreaks of this kind.

With commendable promptitude the public health medical officers discovered the source of the outbreak in meat pies manufactured at a Northants pie factory. How the pies became infected is still a mystery. They contained meat imported from Denmark, and it has been suggested that this may have been contaminated with the organism. But *Salmonella minnesota* is being reported in this country with increasing frequency, and it seems quite possible that the imported meat had nothing to do with the outbreak.

The Salmonella Reference Laboratory, Colindale, identified the first four human cases in Britain of infection with this organism in 1950. In 1951, 23 cases were identified apart from the present outbreak. Most of them were in Inverness and the Aberdeen area, but others were identified in diverse parts of Britain, including one case in London. Two cases in Aberdeen proved to be fatal. On December 10, 1951, the laboratory identified the organism in a specimen taken from a case in Northamptonshire. The possibility of a connexion between this case and the outbreak is no doubt being investigated.

[1] *Mon. Bull. Minist. Hlth, Lond.*, 1951, **10**, 280.

[2] *J. Hyg., Camb.*, 1938, **38**, 716.

This salmonella is so named because it was isolated from a three-weeks-old turkey poult in Minnesota in 1936, and Edwards and Bruner[2] first described its characteristics two years later. In Britain it has not yet been isolated from animals. Whether this outbreak is the herald of more to be caused by *Salmonella minnesota* remains to be seen, but the increasing frequency with which the organism has been identified over the last two years suggests that it may be a new addition to the various groups of organisms apt to cause outbreaks of food-poisoning.

STEROID METABOLISM IN IDIOPATHIC HIRSUTISM

In normal women the urinary excretion of 17-ketosteroids shows no definite variations in the course of the menstrual cycle.[3-7] Pregnanediol, on the other hand, appears in the urine during the luteal phase.[8-9] In women with idiopathic hirsutism Koets[10] found a cyclic variation in excretion of 17-ketosteroids, the peak of excretion coinciding more or less with the probable time of ovulation. Merivale[11] has recently reported similar findings in hirsute women, but by correlating the excretion of 17-ketosteroids and pregnanediol he has shown the peak in the excretion of the former to coincide fairly closely with that of the latter, and to be absent in a hirsute woman who did not ovulate. These facts are of great interest, for casual (and even careful) clinical and laboratory investigations have hitherto yielded negative results and led many observers to conclude that the fundamental defect in idiopathic hirsutism was most likely an excessive response by the affected hair follicles to an apparently normal stimulus—whatever that might be—rather than an abnormal stimulus.

Engstrom and Munson,[12] studying the metabolism of testosterone in normal women, have found that it is converted into 17-ketosteroids to a greater extent during the follicular phase than during the luteal phase—the difference being statistically significant. If it is assumed that the endogenous precursors of the 17-ketosteroids are broken down in the same way, it follows that in normal women more of these precursors are secreted in the luteal phase than in the follicular phase of the cycle. Since their conversion to 17-ketosteroids is less in the luteal phase, the urinary output would remain more or less constant throughout the cycle. Perhaps, therefore, this cyclic fluctuation of 17-ketosteroid precursors is enhanced in women with idiopathic hirsutism, secretion during the luteal phase being even more marked than in normal women. These substances include among their number steroids with androgenic activity, and this train of reasoning leads after all to the suggestion that relatively more androgens are secreted in hirsute than in other women. The situation, however, is not so simple as that. Merivale, for instance, impressed by the coincidence of the peaks of 17-ketosteroid and of pregnanediol excretion in hirsute women, considers that the connexion may not be merely fortuitous, that the substance (measured by the Zimmermann reaction) apparently increasing the 17-ketosteroid output may, in fact, be a 20-ketosteroid (such as a pregnanolone), and that it may thus indicate an abnormality of progesterone metabolism. Engstrom and Munson envisaged yet a further possibility. The conversion of 17-ketosteroid precursors into 17-ketosteroids is regarded as a function of the peripheral tissues—the end-organs, in fact, including perhaps the hair-follicles—and increased conversion may represent an increased response on the part of the end-organs. Such could be the case in hirsute women, their abnormality residing in the failure of the end-organs to decrease their response during the luteal phase. This possibility could be examined by repeating the experiments of Engstrom and Munson in hirsute women; the finding of no difference in the conversion of testosterone to 17-ketosteroids in the follicular and luteal phases would be supporting evidence, provided that the extent of conversion was similar to that found in normal women during the follicular phase.

That the above considerations are nowhere near the whole story is clear from such facts as the absence of any increased 17-ketosteroid excretion—or even decidedly low excretion—in some cases of hirsutism, such as those due to arrhenoblastoma or those associated with bilateral solid enlargement of the ovaries. The field is obviously still wide open for further research.

[3] Werner, S. C., *J. clin. Invest.*, 1941, **20**, 21.
[4] Fraser, R. W., Forbes, A. P., Albright, F., Sulkowitch, H., and Reifenstein, E. C., *J. clin. Endocrinol.*, 1941, **1**, 234.
[5] Talbot, N. B., and Butler, A. M., *ibid.*, 1942, **2**, 724.
[6] Salter, W. T., Humm, F. D., and Oesterling, M. J., *ibid.*, 1948, **8**, 295.
[7] Venning, E. H., and Kazmin, V., *Endocrinology*, 1946, **39**, 131.
[8] —— and Browne, J. S. L., *ibid.*, 1937, **21**, 711.
[9] Cope, C. L., *Clin. Sci.*, 1940, **4**, 217.
[10] *J. clin. Endocrinol.*, 1949, **9**, 795.
[11] *J. clin. Path.*, 1951, **4**, 78.
[12] *J. clin. Endocrinol.*, 1951, **11**, 427.

"FAMILY DOCTOR"

A subscription form for *Family Doctor* was inserted in the *Journal* of December 22, and it is hoped that many doctors will return the forms, filled in, to support this publication of the B.M.A. Designed to be a popular health journal for the lay public, *Family Doctor* made its first appearance in April, 1951, and got off to a flying start. The issues published monthly since then have covered a wide field and have commanded the interest of a steady corps of readers. Medical men and women should find *Family Doctor* a practical magazine which will, by helping their patients, thus help them in their daily practice. The essential function of *Family Doctor* is to promote healthy living both by positive precept and by emphasis on the preventive aspects of medicine. The dish is garnished with articles of popular and topical interest. The January number contains, among its features, "Profile of Niall MacGinnis," by Dr. Cormac Swan; "Surgeons," by Sir Heneage Ogilvie; "Fact and Fancy in Pregnancy," by Professor Dugald Baird; an editorial on hypnotism; and a new poem by Walter de la Mare. General practitioners, in particular, would do a useful service by persuading their patients to become subscribers to *Family Doctor*, which costs only 1s. a month.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE PAINFUL SHOULDER

BY

R. J. W. WITHERS, M.D., M.Ch., F.R.C.S.Ed.

Lecturer in Orthopaedics, Queen's University, Belfast; Orthopaedic Surgeon, Royal Victoria Hospital, Belfast

Pain in the shoulder may result from lesions of a gross nature, such as fractures, dislocations, tuberculosis, bone tumours, and infective arthritis, or may be due to abnormal conditions of the cervical spine, the apex of the lung, and the pleura, or to obstructive lesions of the cervico-axillary outlet. Pain may also be felt in the shoulder from visceral disturbance, notably from heart and gall-bladder disease.

When these lesions are excluded there remains a well-defined group of conditions of the shoulder in which there is pain, limitation or alteration of shoulder movement, sometimes muscular wasting, and usually no radiographic evidence of abnormality. It is to this group that the term "painful shoulder" is applied, and in considering the underlying pathology certain anatomical and physiological features of the shoulder must be recalled.

Normal Shoulder Movement

The movement of full elevation of the arm includes motion at no fewer than four joints: the sterno-clavicular joint is involved mainly in the early phase of elevation, the acromio-clavicular mainly towards the end of this movement, whilst gleno-humeral and scapulo-thoracic movements are occurring throughout all phases. The participation of each of these four components in the entire movement of elevation of the arm is simultaneous and not successive, and each shoulder muscle is known to contract throughout the full range of elevation, though with a peak of maximal contraction at a selective and critical phase.

The muscles acting at the gleno-humeral joint can be divided into two groups—a superficial set, essentially the deltoid, and a deep set consisting of the spinati, the subscapularis, and the teres major and minor. These two groups are separated by the subdeltoid bursa, and each has a different though equally important part to play in shoulder movement. The deep muscles act by tensing, fixing, and depressing the humeral head against the glenoid cavity, so that the superficial muscles, the deltoid, can effect elevation of the humerus at a stable hinge. One set is useless without the other. If the hinge is unstable, as in ruptures of the tendons of the deep muscles, the deltoid cannot elevate the humerus or at best can only do so weakly or incompletely. If the hinge is fixed, "stuck" as it were, by inflammation or adhesions in the deep tendons, elevation is again impossible no matter how powerful the deltoid may be. The deep muscles therefore assume an extremely important position in gleno-humeral movement and their anatomy is worthy of further consideration.

Effect of Advancing Years

In the adult the capsule of the shoulder-joint is fused with the overlying deep muscles, but in the infant these structures are separated by areolar tissue, the tendons being short and the muscle fibres extending to within a few millimetres of their humeral attachments. As age advances the tendons become longer, and the degree of adhesion between them and the capsule also increases, so that in old age the fusion may well be complete. These changes are most marked at the upper part of the capsule, so that in adult life the entire supraspinatus tendon and the upper parts of the tendons of the subscapularis and infraspinatus are intimately fused with one another and with the shoulder capsule. I have called this fused structure the physiological hinge.

Post-mortem investigations have shown that degenerative changes, ranging from superficial fibrillation to complete rupture, of this fused tendino-capsule occur in arithmetical progression as age advances, and that after 75 years fully 50% of all subjects coming to post-mortem examination have incomplete or complete ruptures of the upper part of the fused shoulder capsule. The physiological hinge of the shoulder-joint therefore tends to degenerate as one gets older, and it is suggested that most cases of "painful shoulder" are due to this degeneration, influenced by trauma or by irritative and inflammatory changes in the tendino-capsule itself. Support is given to this suggestion when it is realized that few cases of "painful shoulder" are seen before the age of 45—that is, before the age when degeneration starts. If it is accepted that the pathological changes usually start in the capsule in relationship to the supraspinatus tendon, it is easiest to consider the clinical states produced under an all-embracing term "the supraspinatus syndrome," thereby avoiding the confused and often misleading nomenclature which has been adopted in the past, though never forgetting that other parts of the shoulder capsule are affected by degenerative or inflammatory change in the worst cases.

Clinical Groups

Three groups can be recognized, all painful and each with a characteristic symptom.

1. The arm cannot be elevated by the patient nor can he sustain it in an elevated position when so placed by the examiner, but it drops uselessly to the side. This is the *useless arm or drop-arm* group, and the underlying pathology is a rupture of the supraspinatus tendon.

2. The arm has a full though often weak range of movement at the shoulder-joint, but there is pain with or without partial "locking" of a momentary nature during the middle phase of elevation, or when the arm is descending from the elevated position. This is the *painful arc* group, and the underlying pathology is a partial rupture of the supraspinatus tendon, an irritable area in the tendon due to inflammatory change, an exostosis at the tendon's humeral attachment, or a calcified nodule in the outer part of the tendon itself.

3. The arm cannot be moved actively or passively at the shoulder-joint at all—it is completely "stuck" or, as the Americans so aptly put it, "frozen." This is the *frozen shoulder* group, and the underlying pathology is an inflammatory change in the shoulder capsule.

Useless Arm

The typical case occurs in a labouring man, usually over 45, who after a fall on the shoulder or after attempting to lift a heavy weight experiences sudden diffuse pain in the shoulder, with inability to elevate the arm or to hold it elevated when the examiner places it above a right-angle. A normal range of passive movement is always present on examination and usually tenderness can be found over the tip of the great tubercle of the humerus. The arm is useless, but the pain generally subsides in a few days or weeks. The disability is due to rupture of the supraspinatus tendon, so that there is loss of the power of fixation of the humeral head in the glenoid by the physiological hinge, and the deltoid is thereby put at such a disadvantage that, although it can be felt contracting strongly by the examining hand, it is unable to effect true shoulder movement.

In recent ruptures the loss of fixation may be no more than a reflex phenomenon produced by pain, since the other deep muscles—the subscapularis and the infraspinatus—often uninjured, are also thrown out of action. This can occur in incomplete recent ruptures just as readily as in cases in which the tendon has a complete tear across its substance. It follows, therefore, that it may well be impossible to distinguish clinically beween complete and incomplete ruptures. If pain is abolished by injecting into the subdeltoid bursa a few millilitres of procaine, restoration of shoulder movement will occur in a few minutes in minor ruptures, but in complete ruptures the arm will remain as useless as before. This is a helpful test and easily carried out; helpful, because incomplete ruptures will heal without any special treatment apart from a period of rest, whilst complete ruptures will require surgery.

Treatment

Conservative measures are adopted in the first instance in all cases, and the arm is put at complete rest either in an abduction shoulder splint or else with the arm at the side in a sling or bandaged to the chest wall. There is some difference of opinion about the value of an abduction splint: personally I have not seen any advantage from its use and most patients complain of the awkward and uncomfortable position which it necessitates.

If there is return of some shoulder elevation within four to six weeks conservative measures can be continued and physiotherapy and exercises will complete the return of shoulder function. When no recovery of elevation has occurred in six weeks operation is advised, to repair the ruptured supraspinatus. Several types of rupture can be met with that require slightly different techniques for their repair, which need not concern us here. The aftercare consists of rest for the shoulder with the arm in a comfortable position—I do not now use an abduction splint—until pain and joint irritability have subsided, thereafter active exercises aided by hot packs and assisted movements from the masseuse.

It must be remembered, even though an apparently effective repair of the rupture has been carried out, that the prognosis in complete rupture is still far from perfect; this is especially true if the supraspinatus area shows marked degenerative change at operation. Surgical intervention is often followed by a "frozen shoulder," and it may be six to nine months before one knows what the end-result is to be. This is particularly true in massive ruptures or avulsions of the capsule from the humerus; in these the outlook is extremely poor for the return of useful shoulder function.

Painful Arc

After a fall, or sometimes spontaneously, a painful arc of movement during mid-elevation of the shoulder develops, with weakness of movement which may be mild or may be so marked that the patient is unable to elevate the arm against the slightest resistance from the examiner. When the arm is at the side or in the fully elevated position no pain is felt and there is characteristically a full range of shoulder movement. The symptoms are often mild to begin with, and it may be many months before the patient seeks advice. Patients frequently state that one of their main worries is putting on an overcoat: often they require help with this but are able to carry out other shoulder movements without any difficulty. Sometimes, during elevation of the arm, momentary locking occurs. In time many patients develop trick methods of shoulder elevation to avoid the painful phase, and when both shoulders are examined from the back it often becomes clear that the rhythm of scapulo-humeral action is different on the two sides.

It is thought that the symptoms are due to impingement on the under surface of the acromion process of the outer part of the supraspinatus tendon where there is a tender area from rupture, a granulation tissue swelling, or a calcified nodule. This area is in contact with the acromion only during the middle range of elevation, and so during all other phases, when the two structures are apart, no pain is felt. It is known, however, that the supraspinatus reaches its peak of contraction normally between 80 and 120 degrees elevation of the arm, and it is conceivable that active contraction of this tendon, irritable from rupture or inflammatory change and accentuated by the pull of the tendons fused to it, may generate enough tension to be in itself sufficient to cause the typical pain.

Treatment

Here again conservative measures are adopted at first and consist in teaching the patient how to avoid if possible those movements which cause pain. Repeated injections of procaine into the subdeltoid bursa also help, but it is difficult to see how physiotherapy in any form can effect lasting change. About five out of every six cases eventually clear up whether "treated" or left to their own devices. The remainder should be treated surgically.

The operation is an exploration of the shoulder exactly as for ruptures of the supraspinatus, the acromion process being excised first of all. The supraspinatus area is then examined and when the exact pathological lesion has been identified appropriate surgical techniques are employed. These may consist in excision of a band of adhesions, excision of abnormal calcium deposit, repair of an incomplete tear of the tendon, or excision of an exostosis from the superior facet of the greater tubercle of the humerus. Since it is the impingement of the pathological area against the under surface of the acromion process which is the usual cause of the pain, it is clear that the most important step in the operative treatment is the removal of the acromion. This seems to cause no disability and little or no alteration in the

appearance of the shoulder except possibly in a very thin patient. The aftercare is similar to that described under ruptures of the supraspinatus.

Frozen Shoulder

Half of the cases in this group give a history of direct injury to the shoulder and in the other half the onset is spontaneous and more gradual. Women are affected twice as commonly as men, and the average age is 55 years. At the onset pain may be severe, almost continuous, and felt diffusely over the shoulder. It may radiate down the arm into the fingers, and is usually worse in bed at night. Later the pain becomes less and may only be felt on attempted movement of the shoulder, when it is typically experienced at, or close to, the insertion of the deltoid to the outer side of the humeral shaft. In the early stages all shoulder movements are lost, though, of course, the patient can elevate the arm to about 60 degrees by the gliding action of the scapula on the chest wall; this is, however, purely a scapular movement; true shoulder movement does not occur.

The shoulder gradually loosens, but a period of many months elapses in the average case before there is a return to full shoulder function. In a certain small percentage movement is permanently, though usually only partially, lost. In the average case wasting of the scapulo-humeral muscles can be seen or felt by palpation, though in fat patients this may be very difficult to demonstrate.

It is believed that the essential pathology in this group is inflammation of the capsule after injury or from irritative causes within the supraspinatus area itself such as calcium deposits or the degenerative process already referred to. During the early period of this inflammatory process exudation occurs into and around the capsule, so that fluid is present in the joint and subdeltoid bursa. Limitation of shoulder movement at this stage is mainly due to protective muscle spasm, which therefore relaxes under anaesthesia. When resolution of the inflammation occurs a replacement fibrosis may develop with the formation of adhesions around the capsule, so that there is still limited movement even when the muscles are relaxed under anaesthesia. It is therefore possible in most cases to distinguish between an irritative and an adhesive stage by the simple method of examination of the shoulder under anaesthesia. It is to be expected, of course, that some cases will be partly irritative and partly adhesive if an intermediate stage in the resolution of the inflammatory process has been reached at the time the examination is carried out. This is an important test which should be done in every case of "frozen shoulder," since in the irritative stage the treatment is by rest whilst the adhesive stage calls for active exercise aided by physiotherapy and manipulation. It is clear that in such a tendinous and avascular structure as the shoulder capsule the repair process will be slow and therefore the patient may have to suffer symptoms for many months.

Degeneration or rupture, especially central or partial rupture, of the supraspinatus area of the capsule may be followed by calcium deposition. Such deposits, requiring *x*-ray examination for their discovery, produce symptoms which are no different from those described above and under "painful arc." They are found in about 5% of any series and their presence is clear-cut evidence of degenerative change. Sometimes they set up by irritation a repair process sufficient to effect cure; at others they may rupture into the subdeltoid bursa and produce an explosive onset of pain and uselessness of the arm for a week or ten days, rapidly followed by complete relief from all symptoms. The long tendon of the biceps in its passage through the front of the shoulder capsule may share in the capsular degenerative changes, and these may be so marked that eventually rupture of the tendon occurs.

Treatment

It is important to divide these cases into their subgroups of "irritative" or "adhesive," which, as previously pointed out, is best done by examining the shoulder under anaesthesia. In irritative lesions there is a full range of passive movements, whilst in adhesive cases movement is restricted though it can be freed by manipulation.

In irritative lesions treatment is primarily by rest, support of the arm in a sling being easiest for the patient. There are no real advantages in keeping the arm in an abduction shoulder splint; indeed, this often increases the pain. It has been customary to order heat in one of its various forms, but in a considerable number of cases this treatment may increase the pain and have to be stopped. If complete rest is given to the shoulder the severe pain gradually subsides in four to six weeks, and as soon as this occurs gentle exercises for the shoulder should be encouraged, aided if need be by massage. Exercises are best done while lying down on the back. In the average case return of function may be expected in three to four months, though it will not be full for eight months or even a year in the worst cases. If more vigorous measures are adopted the inflammatory process has no chance to subside and symptoms may persist for many months longer than is necessary.

In many cases replacement fibrosis occurs after the acute irritative stage has passed. At this stage pain is much less severe and usually occurs only on attempted movement. Whilst the shoulder is still "frozen" there is a little movement at the shoulder-joint, so that, along with the scapular glide, the arm can usually be elevated by the patient to about a right-angle. At this stage manipulation of the shoulder under anaesthesia is called for, when full movement can usually be obtained with palpable or even audible "snaps" which are due to adhesions breaking down. The manipulation must be carried out very gently, and, as a first measure, should be through full lateral rotation only. Often one manipulation is enough to free the joint, and it is usually found that after manipulation physiotherapy is a real help in hastening full recovery.

A few cases resist all conservative measures, and for these surgical exploration of the upper part of the joint should be advised, just as has been described for the preceding two groups. In these the subdeltoid bursa will usually be found to be obliterated wholly or in part by adhesions, and after excising the acromion process complete removal of the subdeltoid bursa and the adhesions will be necessary. Manipulation of the shoulder will bring the recesses of the bursa into view, and those adhesive areas which can be seen obviously to be limiting movement will be more readily demonstrated and their excision more accurately carried out. In not more than 5% the shoulder-joint remains permanently "frozen" despite careful conservative and operative treatment. In the other 95% the outlook is good.

VISITING CHILDREN IN HOSPITAL

BY

ALAN MONCRIEFF, M.D., F.R.C.P.

Nuffield Professor of Child Health, University of London; Physician, The Hospital for Sick Children, Great Ormond Street, London

AND

A. M. WALTON, S.R.N., R.S.C.N., S.C.M.

Ward Sister, The Hospital for Sick Children, Great Ormond Street, London

This is a preliminary account of an experiment in visiting that seems to us to be so successful that we want to bring it to the notice of others. It is a plan for daily visiting of children, more particularly those of "toddler" age, by the mothers.

Working at various hospitals over a period of some years, we have been familiar with a variety of patterns for visiting. First may be considered the "no visiting" programme, with an exception made for dangerously ill children. This was probably based mainly upon a fear of introducing infection, but since the British Paediatric Association's investigation (Watkins and Lewis-Faning, 1949) failed to show any correlation between visiting and cross-infection, this fear must be regarded as ill founded. (Visitors are still barred from infectious disease hospitals, in most instances, probably for fear of carrying infection out. Since doctors, nurses, domestic staff, and others in these hospitals "visit" the children and go into the outside world this reason seems a little illogical.) Whatever the reason, this system tended to produce unsatisfactory results. For the short-stay child it meant at least a few days of misery, followed often by a period of partial adjustment, and then, after going home—so we learnt not infrequently—a period of disturbance, although mother had been recognized and welcomed when the time came for discharge.

For children likely to be in hospital for long periods "no visiting" seems to produce the maximum of disturbance. The child forgets his mother, and clings to nurse when the time for discharge comes, so that his return home must be associated with great maternal distress, from the effects of which the child can scarcely escape. Moreover, it was not a satisfactory business for the nursing staff, who tended to develop a possessiveness with regard to the children, the eventual termination of which gave a psychological jolt to both parties.

A modification of the "no visiting" method is to permit parents to look at the children through a glass door or cubicle wall. If this allows the children to see the parents, even accidentally, it can only be condemned as cruel. Even when such accidents did not occur the parents were often very distressed. In wards where this was the custom there was frequent grumbling from nursing staff and from parents, and it never seemed satisfactory.

Daily Visiting

Visiting on "visiting day," once, twice, or even three times a week, is probably all right for older children, say, over 5 or 6 years of age. They can hold out for a few days, even a week, with the knowledge that "mum" is coming again then. For the younger children this is not possible. Their memories are short, and their power of looking forward is short also. This led us to consider daily visiting as a solution. Before describing what in fact occurs it is worth while interpolating some remarks on visiting in general. So often, and not only in children's wards, it seems rather aimless. Mothers do not know quite what to do with the time. They are worried lest anything they do will upset the nursing staff. Therefore it did not seem to us sufficient just to allow visiting daily and leave it at that. The mother must be allowed and encouraged to do certain things to make the visit worth while to all concerned.

The present plan is that mothers are encouraged and even strongly urged to come daily between 5 and 6 p.m. They give the children their suppers, or they feed their infants. They read a story or play a game, clean teeth, hear prayers, and tuck the children down for the night. That is, they do in hospital the things they would do for the children at home. If tears threaten at the time of parting, the mother tries to stay until the child is asleep. If some children are not visited or a mother has to miss a night then some of the other mothers, who are familiar to the children, willingly lend a hand to act as a substitute. The child can look forward to to-morrow. When he first wakes, and for the earlier part of the day, it is not unexciting. New nurses, the doctor's visit, perhaps the visit of the occupational therapist, all help to pass the day, and if homesickness threatens, "mum" is coming after tea. The toddler can understand to-day and to-morrow and can associate things with a meal-time.

We believe that this daily hour spent together by mother and child helps to continue their relationship and does not break up the security which means so much at this young age. The child's needs are being satisfied jointly by mother and nursing staff without the development of abnormal possessiveness or transfer of affection. The mothers are less strained, because they have something to do. If there is some question they want to ask the doctor this is always arranged. (Although not directly associated with visiting, we believe the psychological strain for the parents of a sick child can be eased by making it possible for them to see the physician or surgeon in charge more or less on demand. A time is set aside at the end of each major ward round for this purpose. In fact, parents are encouraged to see the member of the visiting staff concerned and not to be content with what the nursing staff or resident medical officer has to tell them.)

The present method is, of course, supplementary to the presence in hospital of a nursing mother who is breast-feeding her baby. We have also made it a custom for mothers of babies who are artificially fed to come in for longer periods—namely, a day or so at a time—before the infant is discharged, so as to take over full responsibility for the child's care under supervision.

Some Difficulties

It would be unfair to pretend that there are no difficulties in the present scheme. The distance to be travelled daily by the mother, especially in a large city like London, may make daily visiting impossible. There may be other children in the family for whom supervision cannot be arranged. It has always seemed to us a weakness of the method, advocated by others, whereby mothers come in and look after their babies in hospital more or less entirely, that it ignores the rest of the family, especially perhaps the father. It is no gain

to the family relationship if, in saving the child in hospital some degree of psychological trauma, this is inflicted upon others in the family. The daily visiting method seems to share the mother between all those who have a claim on her without being unduly unfair on any.

The present scheme has been in operation for nearly 18 months. Mothers certainly like it. The nursing staff has an opportunity for closer contact with more of the mothers than is possible with any other method, and they also like it. The children seem happy, but clearly some form of follow-up and comparison with other methods is desirable. Children in hospital are part of the large group of children separated (temporarily) from their mothers and deprived of normal home life for a time. It is known that investigation of this larger problem is proceeding here and in other countries. A sponsored investigation of the narrower problem of visiting of children in hospital seems desirable. Meanwhile, without detailed knowledge of what exactly is going on in other hospitals we present this preliminary account of our own trials.

REFERENCE

Watkins, A. G., and Lewis-Faning, E. (1949). *British Medical Journal*, 2, 616.

MEDICAL NEW YEAR HONOURS

The names of the following members of the medical profession were included in the New Year Honours List published in the *London Gazette* on January 1.

K.C.B. (Civil Division)

HAROLD PERCIVAL HIMSWORTH, M.D., F.R.C.P. Secretary, Medical Research Council.

K.B.E. (Military Division)

SAMUEL ROY BURSTON, C.B., C.B.E., D.S.O., V.D., F.R.C.P., F.R.C.P.Ed., F.R.A.C.P. Major-General, Australian Military Forces (ret.).

Knighthood

GEORGE VANCE ALLEN, C.B.E., M.D. Vice-Chancellor, University of Malaya.

WALTER RUSSELL BRAIN, D.M President of the Royal College of Physicians of London.

RUDOLPH ALBERT PETERS, *M.C.*, M.D., F.R.S. Whitley Professor of Biochemistry in the University of Oxford.

C.B. (Military Division)

RODERIC DUNCAN CAMERON, C.B.E., *M.C.*, M.B., Ch.B., Major-General, late R.A.M.C. Honorary Surgeon to the King.

FREDERICK GEORGE HUNT, C.B.E., M.B., B.Ch. Surgeon Rear-Admiral. Honorary Physician to the King.

C.M.G.

JOHN CATARINICH, M.B., B.S. Director of Mental Hygiene, State of Victoria. 1937–51.

WILLIAM ARTHUR EDWARD KARUNARATNE, O.B.E., M.D., M.R.C.P. Professor of Pathology in the University of Ceylon.

C.V.O.

PETER JAMES KERLEY, C.B.E., M.D., F.R.C.P., F.F.R. Director, *X*-ray Department, Westminster Hospital.

ROBERT MACHRAY, M.B., B.S., F.F.A. Anaesthetist, Westminster Hospital.

C.B.E. (Military Division)

EDWARD ALFRED DALEY, M.B., B.S., F.R.A.C.P. Air Commodore, R.A.A.F. Honorary Physician to the King.

ALLAN WATT MCRORIE, M.D., D.P.H. Surgeon Captain, R.N. Honorary Physician to the King.

JOHN CONRAD NEELY, D.M., D.O.M.S., D.O., Air Commodore, R.A.F.

DENIS ADRIAN PRITCHARD, M.B., Ch.M., F.R.A.C.P., M.R.C.P. Surgeon Captain, R.A.N. Honorary Physician to the King.

WILLIAM KILPATRICK STEWART, A.F.C., M.B., Ch.B. Acting Group Captain, R.A.F. Director, R.A.F. Institute of Aviation Medicine.

C.B.E. (Civil Division)

CHARLES CAMERON, M.D., F.R.C.P.Ed., F.R.F.P.S. Professor of Tuberculosis in the University of Edinburgh.

CUTHBERT GAULTER MAGEE, F.R.C.P Ed., Deputy Director-General of Medical Services, Ministry of Pensions.

M.V.O. (Fourth Class)

CHARLES EDWIN DREW, M.B., B.S., F.R.C.S. Chief Assistant and Surgical Registrar, Westminster Hospital.

PETER HENRY JONES, F.R.C.S. Senior Registrar, Brompton Hospital, London, S.W.

CYRIL FREDERICK SCURR, M.B., B.S., D.A. Consulting Anaesthetist, Westminster Hospital.

O.B.E. (Military Division)

JOHN ROBERTSON NIMMO, Major, R.A.A.M.C.

O.B.E. (Civil Division)

MURIEL HELEN DEEM, M.D. Medical Adviser to the Royal New Zealand Society for the Health of Women and Children (Plunket Society).

DONALD CHARLES FARQUHARSON, M.R.C.S., L.R.C.P. Regional Medical Officer, Ministry of National Insurance.

MANUEL LAZARUS FREEDMAN, M.B., Ch.B. Director of Medical Services, Bechuanaland Protectorate.

JOHN MCILRATH GIBSON, M.D. Medical Officer of Health and Chief School Medical Officer, Huddersfield.

ALFRED ERNEST HALLINAN, M.C., M.B., B.S. Regional Medical Officer, Ministry of Health.

WILLIAM ALEXANDER MILNE, M.B., Ch.B. For public and medical services in Greenock.

EDWARD GEORGE MONTGOMERY, M.B., B.Ch. Lieutenant-Colonel, late I.M.S., Surgeon-General, East Bengal, Pakistan.

ALFRED ARTHUR EDMUND NEWTH, M.B., B.S. Senior School Medical Officer, City of Nottingham.

VICTOR EMMANUEL PERERA SENEVIRATNE, M.D., M.R.C.P. Visiting Physician, General Hospital, Colombo.

GEORGE WRIGHT SIMPSON, M.D. Medical Officer and Chief Inspector of Physical Education, Scottish Education Department.

M.B.E. (Military Division)

ROBERT GOUDIE MACFARLANE, M.B., Ch.B. Major, R.A.M.C.

HAROLD STEWART MOORE, M.B., B.S. Lieutenant, R.A.M.C.

M.B.E. (Civil Division)

JOHN CAMPBELL ATHERLEY, M.B., Ch.B. Admiralty Surgeon and Agent, Manchester.

MURIEL JOSEPHINE LOUISE FRAZER, M.D., F.R.C.S.I., M.R.C.P. District Surgeon, St. John Ambulance Brigade, Northern Ireland District.

WILFRED BASIL RALPH JONES, M.R.C.S., L.R.C.P. Medical Officer, District I, Montserrat, Leeward Islands.

RONALD GREAVES LADKIN, B.M., B.Ch. Colonial Medical Service. Medical Officer, Uganda.

WILLIAM RICHARD LAWRENCE, M.B., Ch.B. Medical Practitioner of Te Aroha, Auckland, New Zealand.

An interesting new theory of taste is propounded in *Nature*, December 8, p. 977. It is based on histological study of the olfactory mucosa and taste buds of the rabbit, using new staining techniques which can display the localization of different enzymes, especially various kinds of phosphatases, in different cells. Sections of the nasal mucosa show that all phosphatases are concentrated in three or four basal cells in the olfactory epithelium, while lipases are restricted to Bowman's glands, but esterase is present in all the cells of the olfactory epithelium as well. In brief, a number of enzymes show sharp localization at one or more of six anatomical sites. This has suggested to the authors that substances which are tasted may inhibit the activity of an enzyme in one site, accelerate the activity of another in a second, and have no effect on enzymes in other positions. Inhibition and activation would alter the functioning of local nerve fibres, and thus create a distinctive spatial pattern of nerve impulses transmitted to the brain, and each pattern would represent a separate taste. A similar theory is proposed to account for smell.

Reports of Societies

CRIMINAL RESPONSIBILITY

The Section of Psychiatry of the Royal Society of Medicine held a joint meeting with the Medico-Legal Society on December 11, 1951, at 1, Wimpole Street. Dr. DESMOND CURRAN, the president of the Section, was in the chair. The subject was "Different Approaches to the Problem of Criminal Responsibility."

An extremely interesting evening resulted, limited only by the time available, many of those present being still anxious to contribute to the discussion when the meeting ended at 10.30 p.m. One speaker made a very relevant observation when he said that the witness-box was not a platform from which to ventilate psychiatric theories, and from the general response it was clear that the meeting agreed with this view. The meeting did, in fact, afford a good opportunity for the presentation of the various opinions on the subject without the intrusion of the sensational element usually associated with the ordinary murder trial. Weight was undoubtedly added to the discussion by the obvious experience and authoritative opinion of the various speakers. It seemed that the general opinion was that the M'Naghten rules could not be improved upon, offering as they did a fair legal approach, at the same time the accused's interests being safeguarded by the various other sieves through which his case is passed. One speaker went so far as to declare that psychiatry was not yet in a position to give an opinion sufficiently definite to demand changes in the law. There also appeared to be a strong feeling that, as fitness to plead was not the same as insanity, the case should not be lightly taken from the jury merely because the prisoner showed mental changes.

Fitness to Plead

Sir NORWOOD EAST opened the discussion by indicating that he proposed to deal only with responsibility in cases of murder and in connexion with (1) certification without trial; (2) fitness to plead; (3) guilty but insane; (4) irresistible impulse; and (5) medical inquiry after trial. Throughout his paper he quoted freely from the evidence given before the Royal Commission on Capital Punishment, and emphasized the contrary views expressed by eminent legal and medical authorities. He said that although certification without trial could take place, this in fact rarely did occur. On the other hand, the question of fitness to plead was a common issue to be tried by a jury in England, while in Scotland the so-called plea in bar of trial was frequently decided by the judge alone. He felt that whenever possible the accused should not be deprived of his right to plead and assert his innocence and prove it if possible, and this was particularly applicable when the accused would be left with a feeling afterwards of not having had the opportunity of a full and fair trial. He did, however, feel that he should mention that four experienced prison medical officers had given evidence before the Royal Commission to the effect that they felt that a man, if certifiable as insane, should not be placed in peril by trial. But he added that this did not express the view of some other equally experienced prison medical officers. Divergent opinions on this matter were also expressed by authorities outside the prison service.

The M'Naghten Rules

The issue of insanity at the time of commission of the offence was covered by the M'Naghten rules, which had stood the test of time and defined not insanity according to medical tests but the legal concept of the responsibility of a person for his action. The rules were probably more liberally interpreted nowadays and for that reason had kept up to date with any change in views. At the same time, it was of interest that the British Medical Association, in evidence before the Royal Commission, had agreed with the rules but had suggested that irresistible impulse should be grounds for acquittal. The difficulty, however, was to establish when an impulse is irresistible and when not resisted. In his experience a true irresistible impulse had not been the cause of murder except in association with mental disease, and had then been accepted as ground for acquittal.

The Home Secretary's Powers

Sir Norwood went on to discuss the medical examination which the Home Secretary might order to be carried out by two or three doctors after a person had been convicted of murder, for the purpose of establishing whether he was, or was not, sane at the time of the examination as in contradistinction to the time of the offence. He here quoted an eminent legal authority as having said that it did not seem proper for doctors to express an opinion on a matter which had already been decided by a jury when insanity had been put forward as a defence at the trial, except in very special cases. He himself thought that the method was just and merciful, and would take into consideration any question of mental deficiency. He also mentioned that evidence during such an inquiry was always taken from the prison chaplain and that he had been most impressed by the agreement of the chaplains with the eventual findings.

The Jury

Mr. ANTHONY HAWKE spoke on the legal aspects. He said that the whole basis of the matter was "Justice shall be done" and "Injustice shall not be done." He felt that he had nothing new to add but would like again to stress that the question of criminal responsibility should be left to be decided by the good sense of the fellow men and women of the accused, properly directed and assisted by the lawyers and doctors. If the jury was to be the right tribunal then it was essential to remember what the issue really was—namely, not "Is this man insane?" but "Is he to be held responsible for the act that he has committed?" If this was right, then there must be some sensible and intelligible limits within which criminal responsibility could be measured, and the M'Naghten rules satisfied this as well as anything. He pointed out that the legal principles on which the rules were based had existed long before 1843. He said that the rules had two limbs, the first of which seemed to present no great difficulty—namely, "whether the person understands the nature and quality of the act." The second limb, however—"Did not appreciate at the time that what he was doing was wrong"—was much more difficult. He thought that the second limb would cover the question of irresistible impulse, for if the person thought that what he did was the only possible thing to do, and so must be done, then if this feeling was prompted by a defect of the mind, substantiated by medical evidence, it must come within the second limb. If, on the other hand, it was not prompted by such a defect of reason, then it would seem that the impulse could have been resisted.

Refusal to Plead Insanity

He was strongly in favour of the medical inquiry after conviction in proper cases, and said that he could not agree with the authority who had said that holding such an inquiry after conviction was liable to result in a conflict with the findings of the jury, because what the jury had decided was not that the person was sane but that he had been responsible for the act that he had done. Perhaps it was not realized that unless the accused instructed his counsel to do so a plea of insanity could not be raised, and he himself had had experience of more than one case in which the accused was, in fact, insane (and was so found by the doctors after conviction), but would not allow such a defence to be put forward at the trial.

On the question of the issue of fitness to plead he entirely agreed with Sir Norwood East that a person should not, save in exceptional cases, be deprived of the right to establish his innocence, or for that matter to demand that the prosecution should prove his guilt.

Discussion

Professor E. W. ANDERSON agreed with Sir Norwood East in doubting the so-called irresistibility of impulses. He further said that the extravagance of some of the exponents of this thesis had led psychiatry into disrepute. Finally, after describing an extremely interesting case he had been able to investigate of a well-to-do young man resident in a mental hospital instead of prison, he said that, although he felt that punishment should fit the criminal and not the crime, that end was not always attained by such measures.

Dr. J. C. McI. MATHESON had seen only one case of certification before trial, but he could envisage a person whose mental condition was so serious that he required urgent and immediate treatment. He mentioned that once a person had pleaded guilty to an offence he could be certified only from the prison and not in court. He himself was sometimes surprised by the ease with which the court accepted evidence of unfitness to plead, especially as it involved the risk of an innocent person being detained without trial. He quoted the case of a man with general paralysis of the insane who, although medically certifiable, had contested the charge against him and had been acquitted upon the evidence. Finally, he referred to the electroencephalograph, and pointed out that it could never resolve the question of responsibility.

Dr. T. C. N. GIBBENS, who had studied the problem in the United States of America, said that most States employed a variation of the M'Naghten rules, but there were one or two interesting deviations. In one State there were no tests and the matter of responsibility was treated as fact and decided by the jury, while in another there were two separate trials by jury—one on responsibility and the other on guilt. He suggested that the verdict of "Guilty but insane" was illogical; in America, if you were found insane, you were not guilty. The question of diminished responsibility was covered by the various degrees of murder. He thought the modern interpretation of the M'Naghten rules was broad. The law in respect of provocation was far from being in tune with modern psychiatric views, but no lawyer thought it could be amended.

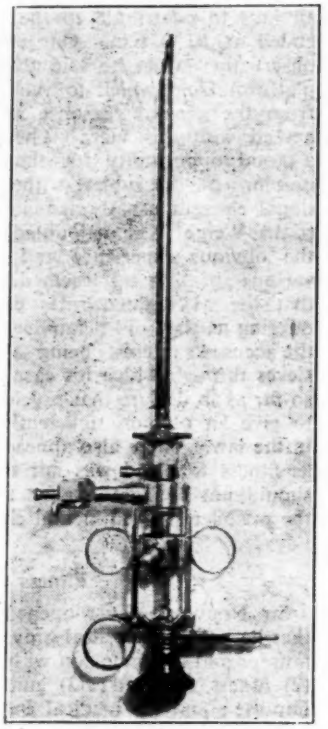
Dr. J. A. HOBSON said that if it was true, as suggested by the opening speakers, that justice was always done, it was not because of the M'Naghten rules but because of the common sense with which the Courts misapplied them. Though he was prepared to believe that insane murderers did not hang, he also believed that justice was not always done in the opposite direction. There seemed no doubt that many sane murderers became Broadmoor patients.

The Minister of Health has approved the appointment of Mr. B. O'Brien to be solicitor and legal adviser to the Ministry of Health in succession to Sir Thomas Harrison, who has retired from the Civil Service. Mr. O'Brien will also act as solicitor and legal adviser to the Ministry of Housing and Local Government. Mr. O'Brien joined the Ministry of Munitions in the first world war and transferred to the Treasury Solicitor's Office in 1920. He became a member of the legal staff of the Ministry of Health in 1929, and has been closely concerned with legislation connected with many aspects of the work of the old Ministry of Health. During the last war he was seconded to the Ministry of Food, where as an assistant secretary he was in charge of supplies of food to hotels, restaurants, and other catering establishments as well as to hospitals, schools, and institutions. Sir Thomas Harrison entered the Ministry of Transport after military service in the first world war, and became an assistant solicitor to the Ministry of Health in 1929. He was appointed solicitor and legal adviser in 1934.

Preparations and Appliances

A ROTATABLE SHEATH RESECTOSCOPE

Mr. J. E. SEMPLE, F.R.C.S., surgeon, St. Paul's Hospital for Genito-Urinary Diseases, London, writes: The importance of being able to resect the anterior part of the prostate gland as easily as the posterior, while manipulating the resectoscope with one hand, has given rise to a demand for an instrument in which the sheath and cutting loop can be freely rotated through a full circle without moving the position of the operating hand. It seemed that this could be most easily accomplished if the metal cone on to which the bakelite sheath is locked could be extended backwards in the form of a metal tube, which would rotate freely within the framework of the instrument and down which the telescope could be inserted. On this metal tube a bobbin of bakelite would slide freely up and down, but rotating with the tube, to which it would be keyed; into this bobbin would be fixed the proximal end of the loop electrode and through it connexion with the diathermy machine would be made.



The main feature of the instrument here illustrated is its extreme simplicity in design and construction. The telescope is of the wide-field, fore-oblique, McCarthy type, which gives an excellent view without loss of definition. In this resectoscope the telescope remains stationary throughout the cut, but if preferred it can be made to withdraw at the end of the cut by the usual mechanism, which is an optional fitting. The cutting loop is controlled by a scissors type of grip, by which the bobbin holding the proximal end of the electrode is advanced or withdrawn by the index and middle fingers while the thumb controls the framework of the instrument. The loop can be made to return automatically to the forward position, after the cut has been finished, by a spring incorporated in the framework, if such is desired, but the control seems more delicate if finger pressure alone operates the loop. The bakelite sheaths are supplied in two sizes for each instrument, F 26 and F 28, so that a urethra of small calibre need not be unduly injured to admit the sheath, yet the advantages of a large-loop electrode are not forfeited. The sheath is attached to the rotating spindle by a ready release-and-lock cone, which makes removal of the telescope and electrode especially easy. The irrigating system is a fixed part of the framework, and is controlled by a wide-bore two-way irrigating tap. The whole instrument can be made boilable.

This resectoscope has been proved to cut very well in all positions and is very pleasant to operate, making the preliminary dissection of the anterior segment of the prostate much easier and therefore more complete.

I have to thank Mr. Lowery and the staff of the Endoscopic Instrument Co., 62, Shirland Road, London, W.9, for their help in constructing this resectoscope.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Death on the Roads

SIR,—I read with interest the report in the *Journal* of December 8, 1951 (p. 1399), of the discussion on "Alcohol and Road Accidents" at the Pedestrians' Association's Conference, November 24, 1951. I agree with many of the points made by various speakers, but it would appear that some statements were made which are ill-founded and may be quite misleading. For example, although it is true that many accidents occur between 10 and 11 p.m. it is not necessarily true that this is due to the advent on the roads at this hour of an increased number of drunken motorists. Perhaps there are more drunken motorists about; perhaps it is simply that there are more motorists about. It may be that there are more drunken pedestrians on the road; or simply that there are more pedestrians. It is very unsafe to come to a definite conclusion that any one factor is responsible for the 10 to 11 p.m. peak.

Indeed, a graph which I prepared some years ago (*Practitioner*, 1945, **154**, 205) showed that there were four peak periods. On week-days the highest peak was between 5 and 6 p.m.; the second highest between 12 noon and 1 p.m.; the third highest between 7 and 8 a.m., and the fourth highest between 10 and 11 p.m. On Saturdays the highest peak was between 12 noon and 1 p.m., and the second highest between 10 and 11 p.m. It is most improbable that the 12 to 1 p.m. peak has anything to do with alcohol consumption, and it is most unwise to assume that the 10 to 11 p.m. peak is necessarily related, solely or even mainly or at all, to the fact that the public houses close about 10 p.m. Cinemas, theatres, and concert halls also disgorge their clients about this time, and it is not only the drunken motorist who is bustling to get home.

The figures on which my references are based were those of the Ministry of Transport Report on *Road Accidents in Great Britain involving Personal Injury* for 1936–7. Now that the five-day working week is fairly widely operative, it may be that more recent figures would show an alteration in the Saturday peak periods.

A further interesting point which emerged from my analysis of the 1936–7 figures was that, whereas there were altogether nearly 173,000 accidents involving car drivers, cyclists, and pedestrians, only 0.8% were definitely attributable to the effect of alcohol in either the driver or the pedestrian, and only 0.3% in which the driver was definitely under the influence of alcohol. A further remarkable fact was that of all the fatal accidents during that period (5,645), there were only 25 in which the car driver was clearly under the influence of alcohol. Of course, as Dr. Goodhart stated, these figures of proved drunken drivers take no account of the large numbers of drivers whose sense of responsibility has been weakened by doses of alcohol which might not be clinically discernible. There is no doubt whatever that an amount of alcohol which is insufficient to cause clinical symptoms, and might be looked upon as not particularly important, can in certain cases produce an effect on the control of the individual.

It seems to me that medical tests in "sub-clinical" cases are of little value. If it is felt that the case against alcohol is sufficiently established, the only course open would appear to be to insist on a blood examination in all cases and to regard the finding of any alcohol at all in the blood as being sufficient to warrant prosecution and conviction. This obviously would mark a serious departure from the present conception of crime and of the rights of the individual, but it would seem to be the only logical way of approaching the problem legally. Motorists would then know that they dare not drink at all if they are in charge of a car, and if they must go out to dinner they must make arrangements for their return home by taxi or otherwise. Whether this proposal is advisable is an entirely different matter.—I am, etc.,

Edinburgh. SYDNEY SMITH.

SIR,—I read with interest the report in the *Journal* of December 8 (p. 1399) of the discussion at the Pedestrians' Association's Conference of November 24, 1951. I have been concerned in the large number of cases of "Drunk in Charge" both at the Metropolitan Police Laboratory and more particularly at the North-eastern Forensic Science Laboratory, and as a result of this experience there are one or two points on which I should like to comment.

First, Dr. A. L. Goodhart, K.C., says that it is not the drunken driver who was the main concern of the meeting. I regret that my experience does not bear this out. Ultimately, I have no doubt this statement may be true, as it is now true in the Scandinavian countries. Unfortunately, in this country we have not yet succeeded in dealing satisfactorily with the drunken driver. In the *Medico-Legal Journal* (1951, **19**, 98) I and my colleagues published a graph of our results on the examination of somewhat over 600 cases, which peaks strongly at 0.30% alcohol in the urine. This means that the drivers had consumed not less than 6 pints (3.4 litres) of a strong beer, such as draught Bass, or nearly half a bottle of spirits. This can scarcely be regarded as a moderate consumption, and this peak of 0.30% is considerably higher than Andresen's peak of about 0.22%.

Secondly, Captain A. Popkess refers to the variation of accident rate with the time of day. Our information is in strong agreement with Captain Popkess's suggestion. The following is a tabulation of the time of arrest of the last 543 cases examined in the counties of Durham and Yorkshire between May 1, 1949, and December 18, 1951. This Table shows that the percentage of the total arrests which occurred during the hours 10 p.m. to 12 p.m. is extraordinarily large. There is also a small hump which would appear to coincide with the afternoon closing hours.

Time	Number
Before noon	4
12 noon to 2 p.m.	1
2 p.m. to 4 p.m.	28
4 p.m. to 6 p.m.	34
6 p.m. to 8 p.m.	29
8 p.m. to 10 p.m.	74
10 p.m. to 12 midnight	263
12 midnight to 2 a.m.	92
2 a.m. to 4 a.m.	16
4 a.m. to 6 a.m.	2
	543

—I am, etc.,

New Scotland Yard, S.W. L. C. NICKOLLS,
Director, Metropolitan Police Laboratory.

SIR,—For many years I was a police surgeon and I have read with great interest the correspondence following the report (December 8, p. 1399) of the discussion on this subject. I fully agree that any reliable test of the alcohol content of either blood or urine would not only act as a deterrent to the dangerous driver who may drive too soon after a party but definitely help to distinguish the real alcoholic, probably sobered by the accident before examination by the police surgeon, from the nervous hysteric whom the fright of an accident may render incoherent.

Whilst, however, not intending to minimize the danger of the loss of fine control and quick reaction after very slight doses of alcohol, I would like to draw attention to the obvious unfairness of any legislation so extreme as is suggested, such as the prohibition of driving within two hours of even one small drink. So many other conditions are, in my experience, at least equally conducive to loss of efficiency in drivers—namely, fatigue, hunger, lack of sleep. It was a matter of regular experience on pre-war Sundays, when road accidents occurred every week, that most

happened between 12.30 and 1.30 p.m. or between 5 p.m. and 6 p.m. I think that hypoglycaemia must be a factor in the "accident prone." It will be most helpful to drivers and to doctors if some observations could be made and published on the complete physiology of the drivers in accidents.

It is pertinent to remind your readers that the question of alcoholism cannot have influenced my observations on the times of accidents, as there are no licensing hours in Wales on Sundays, and we live twenty miles from the border. —I am, etc.,

Ruthin. TREVOR HUGHES.

Fantus Estimation of Urinary Chloride

SIR,—It is still widely believed that the urinary chloride level usually reflects the serum chloride level, and the Fantus test is commonly employed as a guide to electrolyte therapy, especially in surgical practice. Dr. W. H. Taylor has performed a valuable service in drawing attention to the fallacies of the test (November 10, p. 1125). As he points out, however, even more accurate methods of determining the urinary chloride concentration are not necessarily a reliable guide to serum levels. We are particularly interested in those cases, mainly post-operative, in which the urinary chloride concentration is normal or high and yet the serum chloride is low. Following major abdominal operations in children, particularly when there is loss of gastric or intestinal secretions by continuous aspiration, fistulae, or diarrhoea, these findings are not uncommon and are often associated with potassium depletion. Dr. D. A. K. Black (November 17, p. 1207) has described the clinical manifestations of potassium deficiency and the circumstances in which it is liable to occur. In the surgical cases there is excessive potassium loss in the urine as well as in the gastric and intestinal secretions. Potassium is excreted in the urine mainly as chloride, thus leading to a fall in the serum chloride level. Attempts to correct the chloride deficit by enthusiastic infusion of sodium chloride lead to an increasing loss of potassium, mainly in the urine, and a dangerous state of potassium depletion may arise. Diuresis may also occur following such infusions even though the clinical state of dehydration is not fully corrected and may, in fact, even become worse. At this stage the condition may be incorrectly interpreted as being due to sodium deficiency only, and even more sodium chloride may be given, with possibly fatal consequences. As Dr. Black points out, the clinical picture of potassium deficiency may be difficult to assess, but valuable assistance can be obtained from the electrocardiogram, estimations of the serum and red cell potassium, and of the urinary potassium excretion.

The point we wish to emphasize is that potassium deficiency in this type of case is common, at any rate in children, and is often unrecognized. The combination of low serum chloride and high urinary chloride levels should suggest the possibility of potassium deficiency and should call for fuller investigation in order that adequate electrolyte therapy can be given. If these investigations are not practicable potassium therapy, either parenterally in the form of Darrow's solution, or orally, should be carefully considered in all such cases. Although Darrow's solution can be given safely intravenously so long as the rate is not too rapid and renal function is satisfactory, we have found that it may not be sufficient to correct the potassium deficiency and may have to be supplemented by oral therapy.—We are, etc.,

B. E. COHEN. J. T. IRELAND.
Liverpool. E. G. HALL. S. E. KEIDAN.

Hip Reconstruction by Acrylic Prosthesis

SIR,—Many surgeons will have welcomed the letter of Mr. W. Gissane (December 8, 1951, p. 1401), and the warning which he sounded against premature adoption of the method of femoral head replacement for subcapital fractures of the femoral neck. He still favours insertion of the triflanged nail under radiographic control, and expects that this will achieve from 50–60% of successes. Only when this has failed would he resort to the acrylic replacement operation. Dr. R. Judet, who, with his brother and other French surgeons, has developed the use of the acrylic prosthesis, is also emphatically against the general abandonment of the nailing operation in favour of this new method.

The nailing operation, under radiographic control, has always occupied a peculiar position in surgery. If we accept Mr. Gissane's figure of 60% successes, there can be few procedures, outside cancer surgery, where an operation with such modest claims has held its place as the standard procedure for many years. It is an operation of precision and in successful cases gives a perfect result. If unsuccessful, failure is usually complete. It may be said that the nailing operation has remained the standard one because of its very low rate of mortality, even in the very aged, and because there has been no real alternative operation of wide application. Although there have been innumerable contributions to surgical literature on this subject, most of them have been concerned with modifications of technique and new devices for avoiding the causes of failure. Few papers have appeared which have given the long-term results of the nailing operation. Such series as have been reported have, in the main, shown very disappointing results. It is not surprising, therefore, that there should be a ready welcome for what purports to be a promising alternative to an operation which has to admit to a 40% rate of failure.

The most important thing, as Mr. Gissane points out, is that this new operation should be given its trial under the most favourable conditions. That means good selection of cases, a high standard of operative technique, and careful post-operative management in the initial stages. In this latter respect there is a marked contrast to the nailing operation, in which the chief problem of after-treatment has centred on the resumption of weight-bearing.

The results of the nailing operation, in my opinion, have never been adequately reported, and even now it would help to clarify the situation if more results were published. It is greatly to be hoped that a better method may be found for the assessment of the results of the acrylic replacement operation. It should not be difficult for one of the surgical associations to set up a bureau or register to collect data of a large number of subcapital fractures treated by the acrylic method, and their progress at regular intervals. Only by the fullest clinical reporting can an early valuation be made of this new method, which may have such far-reaching possibilities.—I am, etc.,

Guildford. G. N. GOLDEN.

Pre- and Post-operative Treatment of Dehydration

SIR,—Dr. W. H. Taylor's criticism of urinary chloride estimation (November 10, p. 1125) must have been welcomed by many who see it being used as the sole guide to intravenous therapy, especially in the post-operative period. Dr. H. L. Marriott's letter (November 24, p. 1284) must, however, be accepted as a well-balanced survey of the value of urinary estimations in the treatment of dehydration compared with plasma concentrations. He did not, I feel, emphasize sufficiently the fact that in this post-operative or post-traumatic period the widespread faith in Fantus's test can be entirely misleading.

Dr. Marriott suggests that the post-operative retention of sodium is due to a renal attempt to bolster the diminished plasma volume; he therefore suggests plasma *or* saline as a replacement fluid. Saline, however, will be split between the vascular and interstitial compartments, while plasma or plasma substitute will be retained in the vascular compartment. Surely, if any intravenous fluid is to be given during an operation or after other trauma to bolster plasma volume, plasma is always indicated. In view of the many suggested causes of post-operative retention of sodium (Darrow and Pratt, 1950) and the suggestion by many of the importance of an adrenocortical mechanism (Selye, 1949; Wilkinson *et al.*, 1951; Finley *et al.*, 1951) there is further cause for not administering saline in these patients. Finley *et al.* have also shown that there is still sodium retention in patients who have plasma volume maintained by infusions of plasma substitute.

Suggested Scheme of Treatment.—First, we must insist upon the correction of a serious pre-operative defect. To myself, as an

anaesthetist, shock and dehydration are the same thing, and I am glad to see that Dr. Marriott emphasizes this (Marriott, 1951). Let our assessment of the degree of dehydration be based mainly on the history and clinical examination of the patient (which will include the examination of the urine), never forgetting the patient's weight, which I know from personal experience is undoubtedly of the greatest value, as it can be checked easily at frequent intervals.

Pre-operatively, the clinically dehydrated patient of average weight, say 70 kg., should, as a minimum, receive 5 pints (2.8 l.) normal saline, which should include 100 g. glucose to lessen the obligatory urine volume (Gamble) and potassium loss. Where the loss of cation is principally distal to the pylorus, Hartmann's solution may be used.

During operation the anaesthetist will replace blood and treat shock with blood or plasma substitute as indicated and give, where necessary, small quantities of N/5 or N/2 saline to replace visible sweat (and incidentally to keep the drip running). Post-operatively, a basic amount of 5 pints 5% glucose will be given to replace loss by urine and insensible perspiration. Normal saline is only indicated to replace any loss of gastro-intestinal secretion—practically, more accurate than N/2 saline—and to continue treatment of any pre-operative deficit.

Operation is often insisted upon as soon as possible, and therefore the maximum rate of infusion which was recommended by Darrow and Pratt of 2 litres per hour for a 70-kg. man may be used, provided there are no cardiac or other contraindications.

Lastly, potassium deficiency is now well recognized (*Lancet*, 1951, 1, 393) and it is possible that ideally all dehydrated patients undergoing operation should receive potassium. This may be given as Darrow's K-lactate solution at a maximum rate of 80 ml. per kg. per day over a period of four hours by subcutaneous drip, provided there is an adequate urinary volume. Many patients, however, are treated successfully without parenteral potassium therapy, which can be dangerous.

The post-operative progress of the patient should be checked by repeated clinical examinations, which on the average patient will be undertaken daily, coupled with the change in the patient's weight and the fluid-balance chart.

I trust that this letter will provoke further suggestions for the practical treatment of dehydration to assist those who daily have to deal with this problem without expert advice.—I am, etc.,

Twickenham, Middlesex. J. MIDDLETON PRICE.

REFERENCES

Darrow, D. C., and Pratt, E. L. (1950). *J. Amer. med. Ass.*, **143**, 365, 432.
Finley, R. K., *et al* (1951). *J. thorac. Surg.*, **22**, 219.
Gamble, J. L. (1947). *Chemical Anatomy, Physiology and Pathology of the Extracellular Fluid*, Cambridge, Mass.
Marriott, H. L. (1951). In *Medical Treatment*, ed. Geoffrey Evans, Butterworth, London.
Selye, H. (1949). *Practitioner*, **163**, 393.
Wilkinson, A. W., *et al*. (1951). *Lancet*, **1**, 315.

Shortage of X-ray Film

SIR,—At its last meeting members of the Joint Tuberculosis Council expressed their concern about the shortage of *x*-ray film. Causes and remedies were discussed: it was decided to ask for the hospitality of your columns and, if you agree about the urgency of the matter, your editorial support to help overcome the crisis. The manufacturers assure us that output continues at maximum level, but an export quota has to be met before the home market can be supplied. This export quota may amount to as much as between a quarter and a third of the total output. If we were engaged in a non-essential industry we might fairly be expected to accept it, but the maintenance of the health of the population is fundamental to the satisfactory carrying-on of all the other industries in these times of shortage of manpower.

We know that difficulty in obtaining supplies is already interfering with the work of some chest clinics and sanatoria. It will take only a slight further deterioration in the situation to bring about a widespread dislocation in the chest services. We are aware that this is only one aspect of the whole problem of *x*-ray film shortage, but it is the one which touches us most nearly.

The Ministry of Health has stated that the shortage is mainly due to increased consumption. Advancing knowledge in medicine and surgery is intimately bound up with advances in radiology. The wider use which has been made of this specialty has necessitated an increased consumption of *x*-ray film, and this increase must be expected to continue.

We have an incontestable case for urging the Minister of Health to maintain all possible economies, and also to bring all possible pressure to bear on those concerned with the ordering of the export quota to reduce it to a level consistent with the safety of the whole working of the National Health Service. The Minister must be aware that in this matter his interests and ours are the same. His hand will be strengthened and his efforts more likely to be successful if he can show that the hospital service is doing all it can to economize in the use of *x*-ray film in these difficult times.

It is one of the anxieties of this winter that variations in electricity supplies, over which we have no control, may cause many films to be spoilt, and so increase consumption. But there are ways in which we can exercise our ingenuity to make the utmost use of our supplies, and it behoves us all—clinicians, radiologists, and radiographers alike—to see that no unnecessary films are asked for, and that no square inch of film is wasted.—We are, etc.,

PETER W. EDWARDS,
Chairman.
R. L. MIDGLEY,
Hon. Secretary.
Joint Tuberculosis Council.

Exophthalmos

SIR,—I have read with great interest Mr. F. F. Rundle's admirable lecture (December 15, 1951, p. 1433). I would like to put in a plea, however, for Mr. Rundle to qualify one of his statements. He says:

"Should we, or should we not, use the antithyroid drugs? [in the management of the ordinary patient with thyrotoxicosis] I believe the answer is emphatically yes, that we should use the thiouracils in every case of thyrotoxicosis: with the thiouracils the toxic goitre can be quickly converted into a non-toxic goitre. In fact, at the present time, the practical management of thyrotoxicosis should proceed by the following steps. First, all toxic goitres should be converted into non-toxic goitres by antithyroid therapy."

It is the impression of many people interested in the subject that exophthalmos (proptosis) and exophthalmic ophthalmoplegia have become much more frequent in the last few years. About 16 years ago, when Dunhill, Joll, and Keynes were leading in making thyroid surgery safe and popular, exophthalmic ophthalmoplegia after operation was comparatively rare. To-day, it is a much more frequent occurrence; it has also been observed after antithyroid drug treatment. The explanation for this is, in my opinion, based on the pituitary–thyroid axis theory, as mentioned in Mr. Rundle's paper. Thyrotropic (or thyroid-stimulating) hormone is, we now believe, responsible for true exophthalmos and exophthalmic ophthalmoplegia. Thyroid hormone in excess suppresses thyrotropic hormone. Lack of thyroid hormone will upset the balance of the two hormones in favour of "thyrotropism."

Fifteen years ago, when the preparation for partial thyroidectomy consisted in the administration of Lugol's iodine, this caused a temporary concentration of thyroid hormone in the thyroid gland, but did not suppress its production. Hence, there was an antagonist present to thyrotropic hormone in the body. Antithyroid drugs prevent the production of thyroid hormone. Accordingly there is no factor present to act as balance to thyrotropic hormone. Furthermore, subtotal thyroidectomy is much more extensive nowadays. The sudden removal of the larger part of the gland may account for the occasional occurrence of post-operative exophthalmos even in cases prepared only with iodine.—I am, etc.,

London, S.W.3. V. C. MEDVEI.

Post-leucotomy Anxiety

SIR,—Dr. Clifford Allen (December 15, 1951, p. 1463) quotes a case of a leucotomized schizophrenic squandering an inheritance of £7,000, from which he concludes that it is unwise to trust such patients with responsibility, no matter how normal they look. Psychiatrists will agree that this is

a safe precaution, and I have seen several instances of similar disturbed judgments and impaired sense of responsibility in patients discharged following leucotomy, particularly in schizophrenics. One should never regard these patients as absolutely cured by leucotomy. The schizophrenic reaction is more deeply rooted in the constitution than is the case with other types of personality disorder, with the exception of the psychopath.

In contrast to Dr. Allen's supposition of the employer losing money as the result of mistakes made by a leucotomized employee, I would like to quote an actual case of an elderly melancholic shorthand-typist who on returning to work following leucotomy promptly discovered a discrepancy in the firm's accounts despite a recent audit, and consequently saved her employers a sum of over £1,000. It is my experience that undesirable personality defects seldom occur after a lower quadrant leucotomy in the elderly chronic melancholic, and it is in this group of cases that one finds the most successful and gratifying results.—I am, etc.,

Sheffield. F. T. THORPE.

Invite Russian Doctors

SIR,—May I, albeit belatedly, support Dr. R. L. Kitching's proposal (December 1, 1951, p. 1337) to invite members of the Russian medical profession to England? In the present stifling atmosphere of suspicion and denigration it is refreshing to recall that a little good will is entirely seasonable. I should like, however, to ask whether, in the first place, it would really be necessary to arrange such an invitation through diplomatic channels. It seems to me that this would weigh the scheme down with an unnecessary burden of formality. Would it not be possible to communicate directly with the representatives of the Russian medical profession? Secondly, would it be advisable to enforce the principle of freedom to the extent of simply asking the visitors "to say what they would like to see?" I feel that if I, without a word of Russian and with no idea of the organization of Russian life or Russian medicine, were faced with such an invitation to Moscow, I should be more than a little bewildered. Besides, any nation will have features in its life of which it is particularly proud, at which the visitor might perhaps not even guess. Surely it is natural to show a visitor round at first: later he may find things which interest him especially, and ask to see more of them.—I am, etc.,

London, W.8. JOHN MCFIE.

SIR,—The proposal advanced by Dr. R. L. Kitching (December 1, 1951, p. 1337) that we should invite a group of Russian doctors over here is an excellent one. I am sure that such a visit will help to promote good will and that we should be helping in a small way to ease the troubles of a war-worried world. I wonder how many of your readers are aware of the fact that since the war about 10 eminent Russian doctors have visited this country, and during the past two years about six British doctors have visited the Soviet Union? My Society will do all it can to encourage and assist the further development of this interchange of medical delegations.—I am, etc.,

Society for Cultural Relations with the U.S.S.R., London, N.W.10. A. W. LIPMANN KESSEL, Chairman, Medical Committee.

The Doctor and the Courts

SIR,—Dr. George Holloway's letter (December 1, 1951, p. 1339) regarding the Courts' complete indifference to a doctor's responsibilities and commitments at last brings up a matter that should be urgently taken up between the B.M.A. and the Law Society.

I have just had a similar experience at the Assizes held at Winchester. I had to attend at 10 a.m. which necessitated leaving my home at 8.40 a.m. to travel the 38 miles by road. I was kept in suspense for 10 days, and it was only at 4 p.m. on the day before that I received the notice from the plaintiff's solicitor. How is one expected to provide for a locum who could be in time the following morning to see some 20 patients from 9 a.m. onwards? Some patients have travelled from as far as six miles away. The visits for the whole day remained to be done, and a factory appointment for the particular day of the week also had to be attended to, because new entrants had been given notice by post to attend on a particular day at a particular time.

"The Majesty of the Law" needs bringing up to date. Simply because it still has to enforce Acts made in previous centuries there is no reason for the leisurely course of procedure of those times to be maintained. Is it not time that a dictaphone was installed in the court? How long will the Judges of this country continue to write in longhand all that transpires? How often can they hope to keep accurate recordings of the questions and answers of counsel and witnesses?

Later in the day it was found that one of the doctors who had made a recent examination of the patient had not arrived, and I was asked to make a full examination in the jury room. I had to send a policeman to the local hospital for a stethoscope, and wait 20 minutes for it to arrive. After lunch I returned to the court to give further evidence of my latest examination: Counsel decided not to use it, and the Judge released me. I was home again at 4 p.m.

I am sure that most doctors would be pleased if the B.M.A. took these court matters up. Perhaps we would receive a little more respect if the Law realized that the B.M.A. was alive to our problems.—I am, etc.,

Christchurch, Hants. E. F. HUNT.

Criminal Responsibility

SIR,—I must have been one among many in being nauseated recently by reading in the papers that a youth of 19 had been hanged for a callous murder, callous not in the sense of hardened but of unfeeling or without emotion, which at that age is terribly suggestive of schizophrenia.

I suggest that in cases like this, after the question, "Did the prisoner know that what he was doing was wrong?" has been answered by "Yes," a further question, "Was the prisoner by reason of illness or physical defect incapable of *caring* whether his act was right or wrong?" should be put, if not to the jury, at any rate by the Home Secretary to his experts before death is decided on. The essential point is that the atrophy of emotion in schizophrenia can closely resemble that which results from a life of viciousness.

The very articulate but limited legal mind has always shied against the view that criminality can arise from any source except innate wickedness; instinctively it fears that too many of what it considers its lawful prey might escape or be too leniently dealt with for reasons of which its training deprives it of judging the validity. Two further considerations arise:

Continuous efforts should be made to convince our brilliant but slightly case-hardened sister profession that a criminal act is often the first sign of an illness. Many a time in cases of indecent assault counsel have pointed to the humiliated features of a hitherto respectable old gentleman in the dock, when in justice they should have pointed lower down and indicated a large prostate; many a half-cunning theft has been the first sign of a senile dementia. I once came across the case of a young priest who was sentenced for an isolated series of homosexual offences and on admission to prison was found to be suffering from an acute exudative pulmonary tuberculous lesion. Anyone who is familiar with the mental regression in acute toxaemia will recognize this as being, if not the cause of the crime, at any rate so contributory as to verge on condonation.

There is a far more important aspect of this matter than the fate of a few stricken creatures. The abstract idea of Justice in the minds of an educated democracy is enhanced and more revered if it is known that all established knowledge is taken into its cognizance. The figure of Justice, blinded so that she shall better feel the tilt of the scales, is made ludicrous if at the same time she hugs to her bosom prejudices against facts long known.—I am, etc.,

Beckley, Rye. C. G. LEAROYD.

Obituary

A. GARRICK WILSON, M.Chir., F.R.C.S.

Mr. A. Garrick Wilson, senior consulting surgeon to the Royal Hospital, Sheffield, died on December 10, aged 76.

Of Scottish descent, the son of a well-known medical officer of health, Wilson was early imbued with a deep sense of medical responsibility. From Cambridge he went on to St. Mary's Hospital with a university scholarship, and he graduated M.B., B.Ch. in 1899. Deciding to specialize in surgery, he took the F.R.C.S. in 1901 and the M.Ch. four years later. After holding resident posts at St. Mary's he became surgical registrar there. His appointment as senior house-surgeon at the Sheffield Royal Infirmary was followed later by his election to the visiting surgical staff of the Royal Hospital. In the course of the many years that he served this hospital he became widely recognized for the soundness of his work and the thoroughness with which he carried out everything to which he put his hand. No detail was too trivial for his attention if it might possibly contribute towards the welfare of any patient. He had the reputation of a skilful, safe, and tireless operator, but these qualities were dwarfed when laid beside his outstanding attention to the minutiae which so often made the difference between failure and success. In collaboration with his colleagues on the physicians' side he was at his best : courteous, attentive, ready to state a firm opinion, but more than willing to accept a contrary viewpoint when reasonably probable. In carrying out the necessary surgical procedure resulting from a consultation he was loyalty itself. Highly sensitive to any form of injustice or arbitrary use of power, he became sometimes involved in disputes with those whom he considered lacking in full sense of responsibility, and in such respects his annoyance was not easily allayed. But it was generally recognized by his colleagues that any outburst sprang from essentially noble impulses and were untinged by personal envy.

Wilson held many appointments in and near Sheffield. He was lecturer in clinical surgery at the university, orthopaedic surgeon to the Chesterfield Royal Hospital, consulting surgeon to the King Edward VII Hospital for Surgical Tuberculosis, president of the Sheffield Medico-Chirurgical Society, and chairman of the Sheffield Division of the B.M.A. (1924–5). During the first world war he served in the R.A.M.C. as a major.

Among residents, students, and the humbler members of the hospital surgical service Wilson was noted for the care with which he guarded their interests ; he went out of his way to investigate their welfare. In his family and among his more intimate friends he was deeply beloved and respected. Suffering much both in personal ill-health and in bereavement, he bore all with cheerful equanimity. His premature resignation from the staff on account of ill-health left a blank that was deeply felt. In his retirement he was a happy man, enjoying his garden in Beaminster, Dorset, and the simple domestic duties of a country life.—A. E. N.

The death of Dr. N. MOOTATAMBY on November 8 came as a shock to his family and to his numerous friends throughout Malaya. He was born in Ceylon in 1892, but went out to Malaya at an early age. He qualified from the College of Medicine, Singapore, in 1917, and except for the following three years, which he spent in the Johore Medical Service, he was a private practitioner in Johore Bahru for the rest of his life. He was an enthusiastic member of the British Medical Association and took a keen interest in all its activities, being chairman of the Southern Division of the Malaya Branch in 1950–1. He was a true Malayan at heart and gave freely of his services to the country of his adoption, being on numerous committees and boards besides having served three periods of three years each on the State Council of Johore. His services to the Johore State were recognized by the Sultan when he was awarded the Dato Paduka Makota Johore in 1950. In addition to this he was an ideal medical practitioner and a very lovable person, as all his friends know. There must be numerous old Malayans in the United Kingdom who will remember him and regret his death.—C. H. C.

Dr. LUDOLPH BRAUER, emeritus professor of medicine at Hamburg, died on November 25, aged 86. He was educated at Bonn, Marburg, Munich, and Freiberg, and qualified at Heidelberg in 1897. In 1905 he was appointed director of the medical clinic at Marburg. Five years later he became director of the Hamburg-Eppendorf Hospital, a position which he held for many years. In 1919 he was appointed to the chair of medicine at Hamburg, and he also served as rector of the university for some years. Brauer's principal work was in the field of tuberculosis. He was founder and director of the Deutsche Forschungsanstalt für Tuberkulose, and his name is perpetuated in *Brauer's Beiträge zur Klinik der Tuberkulose*, of which he was an editor. He was also joint editor of the *Zentralblatt für die gesamte Tuberkuloseforschung* and of the *Handbuch der Tuberkulose* (Leipzig, 1914–22). He advocated collapse therapy by extrapleural thoracoplasty, and induced artificial pneumothorax by the injection of nitrogen ("Brauer's method"). The treatment of chronic adhesive mediastino-pericarditis by cardiolysis, a procedure now known as "Brauer's operation," was first suggested by him in 1903. Besides receiving honorary doctorates at Bonn, Cordoba, and Shanghai, Brauer was honorary professor of the University of Istanbul and a corresponding member of 51 scientific societies in Germany and elsewhere.

Dr. L. R. J. RINKEL, medical superintendent of the British Legion Sanatorium, Nayland, died on November 10, aged 43. Lambert Ronald Joslin Rinkel was educated at Blundells School, Clare College, Cambridge, and St. Thomas's Hospital. While he was at school it soon became apparent that he would become an athlete of the first rank, and he was in Blundells sports eight. At Cambridge he secured his Blue for the 100-yards in 1929, and he won this event at the Oxford and Cambridge Sports at the White City in 1930. He qualified in 1933, and was appointed to a resident post at St. Thomas's Hospital. At this time he became seriously ill with tuberculosis, and after his recovery he specialized in diseases of the lungs, holding appointments at the Royal National Hospital, Ventnor, and the Kelling Sanatorium, Holt. In 1946 he was appointed medical superintendent to the British Legion Sanatorium at Nayland.

S. A. P. writes: Ronnie Rinkel will be sadly missed by his many friends: he had accomplished much in his short span. I first knew him at Cambridge, where he won renown as a sprinter. He was a gay and amusing companion as a student, and a conscientious worker. In those early days the strong character which was to stand him in good stead in later trials was already evident. At St. Thomas's Hospital, where he found quite a number of his old Cambridge friends, he quickly made many new ones and took a full and active part in the hospital's corporate life. After qualification he was appointed to one of the coveted resident posts, and was a most popular member of "College House." It was during this, his first job, that he developed pulmonary tuberculosis. Gloom descended on College House when the desperate situation was understood; his past athletic career added starkness to the event. But he

faced what seemed hopeless odds most courageously—one operation followed another, but for long we had no good news. Contrary to expectations, he recovered, as he himself had never doubted he would. I met his future wife when he was recovering and understood what her staunch support had meant to him. His long illness probably helped him a great deal to know the disease in which he later specialized, and made him the understanding doctor he was. Our paths diverged, but I heard from time to time of the good work he was doing at Kelling Sanatorium, Holt, and later at Ventnor. In 1946 he was appointed medical superintendent to the Nayland Sanatorium, and it was a delight to welcome to one's own neighbourhood an old friend who, one knew, would add so much to the local fraternity. His worth was soon appreciated in the Essex–Suffolk countryside, and, though he was only with us a few years, his parting leaves an irreplaceable gap among his doctor friends. He will be deeply mourned by the past and present sanatorium patients whom he served so well. It is sad indeed that when he had won such a notable victory over tuberculosis his brave heart yielded at last to hypertension. Our kind thoughts go out to his wife and to his two children.

THOMAS LANDLES GORDON, surgeon to out-patients in the Western Infirmary, Glasgow, died in the Gardner Institute of Medicine on November 29, aged 49. Tom Gordon was educated at the Glasgow Academy and the Glasgow University, graduating M.B., Ch.B. in 1925. While he had an early leaning towards surgery, it was not until the middle nineteen-thirties that he finally adopted surgery as a career and joined the staff of the Western Infirmary. He became a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow in 1937, and a Fellow of the Royal College of Surgeons of Edinburgh in 1938. It was obvious before long that he was a surgeon of great promise. From the very outset his judgment was sound and his manipulative dexterity rapidly became of a high order. His most comforting attribute was his absolute reliability. During the second world war he was a tower of strength in the unit to which he was attached. He was an indefatigable worker, and his strong physique made him appear untiring. He was a most helpful and considerate colleague and a recognized guide, philosopher, and friend to the younger members of the staff. He was a capable teacher and a penetrating clinician. For a period he served as an examiner for the triple qualification on behalf of the Royal Faculty. He was an all-round sportsman. In his youth he excelled at rugby football (he was a notable forward for Glasgow Academicals in their halcyon days), cricket, swimming, and tennis. Later he took up golf and became a scratch player. In 1949 he was captain of the Western Golf Club at Gailes, and in that same year he had the added distinction of being the champion of the club. His untimely death came as a stunning blow to his colleagues and friends. On December 1 a funeral service was held in the David Elder Memorial Chapel of the Western Infirmary, where a large congregation of colleagues, friends, and West of Scotland golfers fully testified to the regard and respect in which he was held by the community. Mr. Gordon is survived by his wife, to whom we offer our deepest sympathy.—A. J. H.

The Services

Surgeon Lieutenant-Commander I. G. W. Pickering, R.N.V.R., has been awarded the R.N.V.R. decoration.

Brigadier (Temporary Major-General) J. C. Collins, C.B.E., late R.A.M.C., has been appointed Honorary Surgeon to the King, in succession to Major-General J. M. Macfie, C.B., C.B.E., M.C., late R.A.M.C., retired.

Colonel (Temporary Brigadier) Albert Sachs, late R.A.M.C., has been appointed Honorary Physician to the King, in succession to Major-General K. A. M. Tomory, C.B., O.B.E., late R.A.M.C., retired.

Medico-Legal

DIVORCE FOR INCURABLE INSANITY

"Continuously Under Care and Treatment"

By Section 2 of the Matrimonial Causes Act, 1937, a divorce petition can be founded in England on the ground that one party to the marriage is incurably of unsound mind and has been "continuously under care and treatment" for a period of at least five years immediately before the presentation of the petition. Being under care and treatment includes detention pursuant to inquisition or order under the Lunacy or Mental Treatment Acts, or order or warrant under the Naval Discipline Act or Army or Air Force Acts, detention under the Criminal Lunatics Act, and treatment as a voluntary patient under the Mental Treatment Act, 1930.

The Court of Appeal recently[1] had to decide the meaning of "continuously" on an appeal by a husband whose petition for divorce on the ground of incurable insanity had been dismissed. The wife first came under care and treatment on admission to a mental hospital in October, 1945. Her condition did not improve, and she was discharged and removed to a hospital in Scotland, where she remained under detention until March, 1948. She then came to London, and was within a few days admitted to hospital in Surrey, where she had remained until the petition was presented. Mr. Commissioner Bush James dismissed the petition on the ground that the wife was not under detention during the journey from one hospital to another, and therefore had not been "continuously" under care and treatment for the necessary period.

The Court of Appeal allowed the husband's appeal and granted him a decree. The Lords Justices held that the period of detention in Scotland could be added to the periods in England, and that it was not the intention of Parliament that the five-years period of detention should be broken by the removal of the patient from one hospital to another.

[1] *Scotsman*, July 7, 1951.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

Denis Haigh Marrian, Ph.D., has been appointed an Assistant Director of Research in Radiotherapeutics, from October 1, 1951.

The Raymond Horton-Smith Prize for 1950–1 has been awarded to Dr. Hugh Reginald Jolly for his essay entitled "A Study of Sexual Precocity." *Proxime accessit*: Dr. J. A. R. Miles, for his essay on "Diet and Exercise in Relation to Certain Infections."

In Congregation on December 15, 1951, the following medical degrees were conferred:

M.D.—N. C. Lendon, D. H. Mackenzie, B. F. Brearley, H. B. Dodwell.

M.B., B.CHIR.—H. A. Sanford (by proxy), Patricia L. Broadhead (by proxy).

UNIVERSITY OF GLASGOW

On December 5, 1951, the degree of M.D. (with commendation) was conferred *in absentia* by diploma upon J. Vaughn, M.B., Ch.B.

UNIVERSITY OF EDINBURGH

At a Graduation Ceremonial on December 14 the following medical degrees and diplomas were conferred:

M.D.—[2]P. F de Caires, [1]R. McK. Fulton, [2]C. E. L. Haffner, [2]T. Harrison, H. Oswald-Smith, A. S. L. Rae, [1]A. R. Somner.

PH.D.—*In the Faculty of Medicine:* D. P. Basu, M.B., B.S., A. S. Outschoorn, M.B.

M.B., CH.B.—Audrey N. H. Andrew (née Robertson), W. R C. Andrew. E. S. Blackadder, F. K. P. Brydon. R. C. Buchanan, Isobel C. Campbell, G. M. Dewar, J. M. P. Dippenaar, W. F. M. Dorward, [2]Margaret J. Field, P. T. Fraser, P W. E. Hayward, R. S. Jarema, J. H. Jennings, D. F. Kerr, Margaret L. Liddell, D. W. Lyon, Mary I. McArthur, R. Macdonald, M. A

McFadyen, D. W. Maxa, A. E. Meek, C. C. Moir, G. D. E. Morris, J. E. Munro, A. E. M. Reekie, W. D. Riddell, A. A. Robertson, A. H. I. Scott, W. A. Simpson, R. M. Stewart, J. H. Sutherland, G. P. Syme-Thomson, J. M. Tainsh, Jean C. Taylor, C. G. M. Third, F. A. Viapree, F. E. B. Wills.

DIPLOMA IN MEDICAL RADIODIAGNOSIS.—A. Lien-yiu Chen, J. MacG. McKay, M. K. Mitter.

DIPLOMA IN MEDICAL RADIOTHERAPY.—W. D. Rider.

The following scholarships, bursaries, and prizes were awarded in the Faculty of Medicine: *Vans Dunlop Scholarship in Forensic Medicine and Obstetrics*, J. P. Laidlaw. *James Cropper Scholarship and Waldie Griffith Prize Scholarship*, Rena E. Hogg. *Andrew Graham Ritchie Bursaries*, A. W. McKenzie and Margaret A. Loraine. *Mackie Bursaries*, A. J. Duff and K. McL. Stewart. *Coldstream Memorial Medical Missionary Bursary*, A. B. Partridge. *Llewellyn Bevan Prize*, J. F. O. Mitchell, M.D. *Russell Crighton Prize*, Margaret A. Loraine.

[1]Highly commended for thesis. [2]*In absentia*.

UNIVERSITY OF DURHAM

In Congregation on December 14, 1951, the following medical degrees were conferred:

M.B., B.S.—J. R. B. Ball, E. I. Blenkinsop, R. Bruce, G. Y. Caldwell, A. I. A. Charlton, Z. H. Cywicki, J. Dixon, J. Fitzgerald, Joyce H. Hindmarsh, W. Holmes, W. E. J. Kirby, P. H. D. Lewars, J. B. Lilly, Jean M. McIvor, J. F. Mather, F. C. Pickering, I. R. Pyle, J. B. Richardson, T. M. C. Saint, W. A. Shiells, Margaret Sibson, H. Tubmen.

UNIVERSITY OF LONDON

Dr. Charles Felix Harris has been appointed representative of the Faculty of Medicine on the Senate for the remainder of the period 1950–4, in place of the late Mr. J. B. Hunter.

The following have been appointed, or nominated for appointment, or reappointment, as representatives of the University on the governing bodies indicated in parentheses: Professor W. D. Newcomb (Institute of Orthopaedics); Professor J. M. Mackintosh (London School of Economics and Political Science); Mr. P. H. Mitchiner (Royal College of Veterinary Surgeons); Dr. C. F. Harris (School of Pharmacy).

The appointment of house-surgeon to the neurosurgery department at the London Hospital has been approved for the purposes of Branch I of the M.D. examination.

Dr. Norman Henry Ashton has been appointed to the University Readership in Pathology tenable at the Institute of Ophthalmology, from January 1, 1952.

Dr. Ian Donald has been appointed to the University Readership in Obstetrics and Gynaecology tenable at the Postgraduate Medical School of London and attached to the Institute of Obstetrics and Gynaecology, from January 1, 1952.

The title of Reader in Veterinary Physiology in the University has been conferred on Hans Friedrich Rosenberg, M.D., Ph.D., in respect of the post held by him at the Royal Veterinary College.

The following candidates have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN MEDICAL RADIOLOGY (DIAGNOSIS).—P. Purcell, Una Scorer, R. F. Stubbs, Tha Din.

ACADEMIC POSTGRADUATE DIPLOMA IN MEDICAL RADIOLOGY (THERAPY).—Ethel P. Johnson.

UNIVERSITY OF MANCHESTER

The following candidates have been approved at the examinations indicated:

FINAL M.B., CH.B.—*Old Regulations:* J. R. Jaffe, D. W. Preston. *New Regulations:* J. Ashworth, F. N. Bamford, Freda A. Broadhurst, Barbara Clough, E. M. Coates, J. Cragg, L. Duggan, J. H. A. Dwek, Margaret J. Foulds, P. Fulton, P. W. Gilman, T. T. Glancy, E. N. Gold, Dorothy M. Gratton, P. G. Haddock, C. S. Hajikakou, E. G. R. Jones, R. J. Lande, J. B. Law, B. E. Marks, G. H. Mazey, Elsa M. Mellor, G. W. H. Oldfield, L. Poller, H. J. Reynolds, G. B. Ross, D. Rothwell, G. J. Ryder, F. Smith, G. F. Smith, O. T. Taylor, P. R. Ward, W. A. Whittaker, A. Withnell.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—H. S. Coulsting, M. M. Lidgate, Edith M. Thorp.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examinations indicated:

M.D.—K. McCarthy, I. P. Madhok, H. Roberts.

M.CH.ORTH.—W. J. Betts, P. Chandra, K. R. Daymond, G. F. Fischer, F. J. Gruar, D. R. Gunn, A. K. Gupta, M. Natarajan, J. A. O'Garra, J. S. Roarty, I. W. Winchester, W. H. de W. de Wytt.

FINAL M.B., CH.B.—*Part IV:* Jean D. Birtles, J. H. G. Brown, R. W. H. Clarke, Josephine Dec, K. M. Fraser, B. Freeman, Morilee Garside, Pamela Garside, K. C. Greenwood, F. R. Howell, Roma McDonald, J. J. D. Macpherson, Marianne A. A. Phillips, M. A. H. Rayman, S. J. Rogers, J. A. Seddon, Ellen G. Williams, D. Winter. *Part III:* Elizabeth Bownass, W. E. Cooper, G. Corney, Enid C. Davies, J. C. Denmark, A. J. Entwistle, L. A. Guile. F. B. Hartley, Margaret J. Hellaby, N. St. J. Hennessy, Joan Knowles, A. M. Laylee, I. Miller, S. Naylor, L. A. Nettleton, W. G. W. Parry, H. G. Row, W. A. Weston, A. H. Wilde, J. D. Wright.

D.P.H.—*Part I:* M. S. Boparai, D. Brahott, J. L. Cotton, Hla Han, V. Israngura Na Ayudhia, O. Jitavare, N. N. Kanyarutoke, A. R. Kennedy, E. Lutfi, Lillie L. Munro, R. Muscat, R. C. O'Grady, W. H. Parry, T. Sukhanenya, T. A. J. Thorp, K. O. Torgersen, P. H. Waage.

CERTIFICATE IN PUBLIC HEALTH.—H. Frederiksen, E. F. W. Richards.

UNIVERSITY OF BRISTOL

The following candidates have been approved at the examinations indicated:

FINAL M.B., CH.B.—C. Barwick, Audrey M. Blake, G. V. Catford, Ann M. Haines, G. J. Hillier, R. J. Hunt, D. J. A. Jarvis, June P. Lawson, Mary Motton, I. C. Murison, P. Norris, A. J. Rowland, N. Sartori, M. Sheldrick, N. C. Tricks, D. W. Trump, D. W. Wright. *In Group I completing the examination:* R. A. Iles, M. H. B. Joyce, Gillian F. Peacock. *In Group II completing the examination:* Denise G. Macleod, Antonina J. Sidorowicz. *In Group II (Surgery and Obstetrics) only:* Helena B. M. Bailey, S. H. Brown, A. G. Walker.

CONJOINT BOARD OF IRELAND

The following candidates were duly admitted licentiates in medicine and midwifery on December 7, having passed the final examination in medicine, surgery, and midwifery of the Conjoint Board of Ireland: A. S. Beilin, F. Coyne, Anita C. Doherty, J. E. Flanigan, R. F. Frost, N. L. G. Gough, Mary M. B. Hillery, B. J. P. Leahy, Maire M. P. Leahy, M. J. Murphy, Mary P. Murray, G. J. McManus, D. J. O'Kelly, E. O'Neill, D. O'Reilly, J. F. X. O'Sullivan, Katherine P. Prendiville, B. D. Quigley, Mary T. C. Rahill, M. J. Ryan, M. Ryan, W. A. Ryan, J. P. Stewart, R. A. Wade.

The following candidates have been approved at the examinations indicated:

DIPLOMA IN ANAESTHETICS.—C. A. G. Armstrong, J. C. Clarke, Patricia Delany, E. A. Frayworth, L. McArdle, J. A. McNeilly, Patricia O'Neill, J. H. Tyrrell, N. Zwick.

DIPLOMA IN CHILD HEALTH.—V. Barry, D. C. J. Carter, G. Cremer, C. P. Nanavati, W. P. O'Keeffe, K. J. Quinn, Carmel P. Ryan.

ROYAL SOCIETY

The Council of the Royal Society has appointed Alan Lloyd Hodgkin, F.R.S., to be a Royal Society Research Professor from January 1, 1952. Mr. Hodgkin will continue to work at the physiological department of the University of Cambridge on the processes of excitation and conduction in nerve.

Vital Statistics

Salmonella Minnesota Infection

A large outbreak of food-poisoning caused by *Salmonella minnesota* has occurred in Northamptonshire and the surrounding country. Several hundred people have been affected, and a man and a woman have died. The source of infection has been traced to meat pies manufactured at a pie factory in Northamptonshire. In nearly all cases the symptoms are very mild, lasting for about three days. They include headache, nausea, and diarrhoea, and the patient is often left feeling rather depressed. As is usual in such outbreaks, elderly people are more liable to show symptoms of infection than the young. The incubation period is about 18 hours.

The first case was identified on December 21, 1951. The source was traced the next day and immediate action taken. No fresh cases are known to be occurring now. The precise origin of the infection in this outbreak is not yet known—that is, how the meat pies came to be infected.

They contained meat imported from Denmark, but that cannot necessarily be incriminated, for *Salmonella minnesota* is by no means unknown in Britain. We are grateful to the Salmonella Reference Laboratory, Colindale, for informing us that on December 10 this organism was identified by the laboratory in a specimen obtained from a patient in Northamptonshire.

In 1951 this laboratory identified the organism in 23 cases before the Northamptonshire outbreak. Most of them came from Inverness and the Aberdeen area. Two fatal cases in Aberdeen were identified in October. The infection was also identified in a case in London in November. In 1950 four human cases were discovered, but no case is known to have occurred in Britain before that.

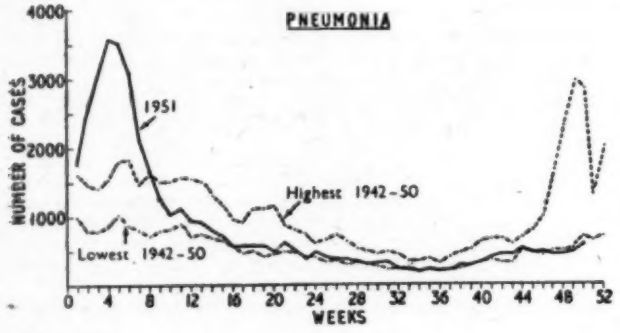
Salmonella minnesota was isolated by Dr. B. S. Pomeroy in 1936 from a three-weeks-old turkey poult in Minnesota and its characteristics were first described by Edwards and Bruner (*J. Hyg., Camb.*, 1938, **38**, 716). This is the first large outbreak in Britain known to be caused by this organism.

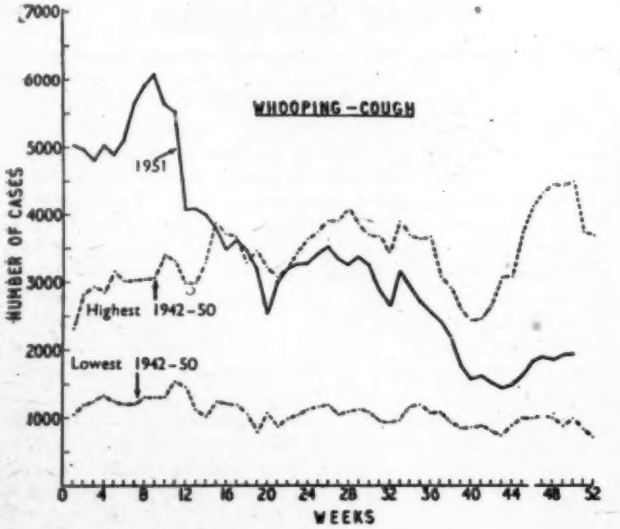
Week Ending December 22

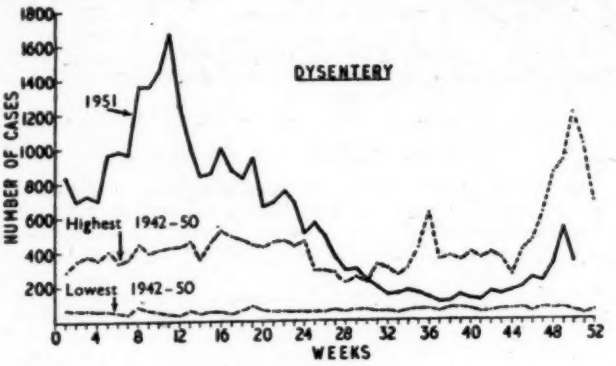
The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,552, whooping-cough 1,819, diphtheria 54, measles 2,321, acute pneumonia 681, acute poliomyelitis 28, dysentery 422, paratyphoid fever 17, and typhoid fever 6.

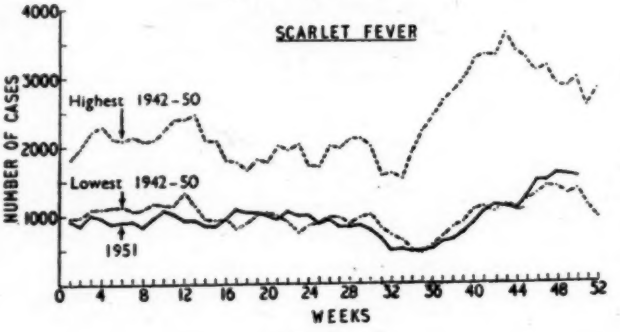
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus -------, the figures for 1951 thus ———. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The chief fluctuations in the trends of infectious diseases in England and Wales during the week ending December 15 were increases in the number of notifications of acute pneumonia 121 and measles 104, and a decrease of 200 for dysentery.

Only small variations were reported in the trends of scarlet fever and whooping-cough; the totals for these diseases were 18 and 1 respectively fewer than in the preceding week. The rise in the incidence of measles was contributed by the midland counties; elsewhere a small decrease occurred. The largest increases were Warwickshire 128 and Staffordshire 73, and the largest decrease was Yorkshire West Riding 56. The notifications of diphtheria were 12 more than in the preceding week. The largest of the local fluctuations were rises in Lancashire 9 and Warwickshire 4, and falls in Staffordshire 6 and Yorkshire West Riding 4. A small rise in the incidence of acute pneumonia was reported from every region of the country except London.

Of the 17 cases of paratyphoid fever 10 were notified in Suffolk (Stowmarket U.D. 7).

The number of notifications of paralytic acute poliomyelitis were 1 and non-paralytic cases 8 fewer than in the preceding week. The largest returns during the week were: Middlesex, 7; Lancashire 5; Cambridge, Cambridge M.B. 4; Warwickshire, Birmingham C.B. 4; Kent, 4.

A further 104 cases of dysentery were notified in Norfolk, Norwich C.B. This brings the total cases for this city up to 446 for the past four weeks. The other large returns of dysentery were London 43, Middlesex 40, Lancashire 19, County of Southampton 17, Warwickshire 13, and Northumberland 11.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in November was 122, compared with 139 in the previous month and 155 (revised figure) for November, 1950. Of these deaths 16 were underground in coal mines and 23 were in building operations.

The following cases of industrial disease were notified during the month: lead poisoning 8, mercurial poisoning 1, anthrax 2, epitheliomatous ulceration 18, chrome ulceration 50; total 79. There were no deaths (*Ministry of Labour Gazette*, December, 1951).

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **December 15** (No. 50) and corresponding week 1950.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 126 great towns in England and Wales (London included), London administrative county, the 16 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 13 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1951					1950				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	42	2	12	1	4	50	4	11	2	2
Dysentery	337	43	39	1	2	1,214	52	147	7	
Encephalitis, acute	7	1	0	0	1	6	1	1	0	
Enteric fever:										
Typhoid	1	0	0	0	0	2	0	0	0	0
Paratyphoid	17	0	7(B)	0		5	0	3(B)	0	
Food-poisoning	55	13		0		95	11		1	
Infective enteritis or diarrhoea under 2 years				13	18				10	18
Measles*	2,448	16	139	179	98	14,223	1534	255	100	157
Meningococcal infection	29	3	14	2	4	29	0	14	1	1
Ophthalmia neonatorum	37	3	5	0	1	23	0	12	1	
Pneumonia†	583	30	183	9		684	36	291	10	
Poliomyelitis, acute:										
Paralytic	36	1	8	0	3	107	5	6	1	4
Non-paralytic	8	0								
Puerperal fever§	226	35	5	0	1	66	3	16	0	
Scarlet fever	1,543	131	312	31	44	1,348	101	203	37	82
Tuberculosis:										
Respiratory			136	30				131	35	
Non-respiratory			29	5				31	7	
Whooping-cough	1,929	51	324	57	88	4,503	424	620	35	68

DEATHS in Great Towns	1951					1950				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery		0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	1	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	5		3	0	3	26		3	2	1
Influenza	17	3	2	0	0	33	2	6	0	0
Measles		0	0	0	1		0	0	0	2
Meningococcal infection		0	2				0	0		
Pneumonia	192	33		8	6	283	38		21	7
Poliomyelitis, acute	2	0			0	8	2			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	151	22	21	5	7	167	21	38	5	14
Non-respiratory		2	1	1	1		4	7	1	0
Whooping-cough	3	0	0	0	0	9	1	0	0	0
Deaths 0–1 year	230	33	25	10	15	258	27	37	17	21
Deaths (excluding stillbirths)	5,119	855	600	122	154	6,080	924	789	172	234
LIVE BIRTHS	6,161	1000	768	187	328	6,436	1092	823	190	261
STILLBIRTHS	167	26	20			178	22	28		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Dr. N. Gerald Horner

Dr. Horner, who was Editor of the *British Medical Journal* from 1928 to 1946, celebrated his 70th birthday on Tuesday, January 1. A message of congratulations was sent to him from the staff of the *Journal*.

Government Scheme for Refresher Courses

Many general practitioners are not aware that, subject to certain conditions which are readily satisfied, they are entitled to 22 half-day sessions of postgraduate refresher work in each academic year. This can be spent as a fortnight's whole-time attendance at a refresher course, or the period may be split up in a variety of ways, of which attendance once a week is one example. Refresher courses are organized by the universities in each hospital region throughout the country, and the fees for approved practitioners are paid by the Ministry of Health through the university which sponsors the course. Doctors attending courses under this Government scheme can claim travelling expenses. Where absence from home is necessary or a locum is needed during attendance on a whole-time course, they can claim subsistence allowance and a grant towards the expenses of a locum. These courses are advertised in the medical journals from time to time, and the postgraduate dean or director in any university will always give information on the postgraduate facilities in his region. In last week's advertisement columns will be found the programme of courses so far arranged for 1952 by the British Postgraduate Medical Federation (University of London). These courses are open to approved practitioners from any part of the country.

Chelsea Clinical Society

The third meeting of the 55th session was held on December 11, when a discussion on "The Doctor in the Magistrate's Court" was opened by Sir Laurence Dunne, the senior metropolitan magistrate, and Dr. Philip Addison, assistant secretary of the Medical Defence Union. The date of the next meeting was announced as January 15.

St. Thomas's Day Service

The 400th anniversary of the refounding of St. Thomas's Hospital was commemorated by a service held at Southwark Cathedral on December 21, 1951, attended by the Queen and Princess Alice. The Archbishop of Canterbury reminded the congregation that the cathedral was the original priory church of the hospital, which was founded for a second time in 1551 by Edward VI after it had been plundered by Henry VIII. The Bishops of Southwark, Kingston, and Woolwich took part in the service and paid tribute to various people who had helped to develop and support the work of St. Thomas's, including Florence Nightingale, who established her school of nursing in the new buildings.

Harveian Society Prize Essay

Jaundice is to be the subject for the Buckston Browne Prize Essay. The prize, consisting of a medal, together with the sum of £100, will be awarded for the best essay on the subject, and is open to any member of the medical profession registered in the British Isles or Dominions, and is limited to candidates under 45 years of age. Essays must be sent in by December 1, 1952, and further particulars may be obtained from the hon. secretaries, the Harveian Society of London, 11, Chandos Street, Cavendish Square, W.1.

American Journal of Tropical Medicine

The American Society of Tropical Medicine and the National Malaria Society have both been dissolved and are to be replaced by a new body, the American Society of Tropical Medicine and Hygiene. The respective journals of these organizations have been amalgamated to form the *American Journal of Tropical Medicine and Hygiene, incorporating the Journal of the National Malaria Society.*

Louis Braille

On January 6 occurs the centenary of the death of Louis Braille. He was 42, and had been blind from birth. By his introduction of the system of embossed types he made the greatest single contribution ever devised to compensate for the handicap of blindness. He actually modified a system which had been invented by Charles Barbier in 1820, and he first publicly expounded it in 1829, while his book on the subject, *Procédé pour Ecrire au Moyen des Points*, appeared in 1837. Braille symbols each consist of a series of up to six dots arranged like the dots on a domino, and giving a range of combinations enabling all the letters, punctuation signs, etc., to be represented.

Royal Faculty of Physicians and Surgeons of Glasgow

The President and Fellows of the Royal Faculty of Physicians and Surgeons held their biennial dinner in the Faculty Hall on December 7, with the President, Mr. Walter W. Galbraith, in the chair. There was a large attendance of Fellows and guests. The principal guest was the Rt. Hon. James Stuart, M.P., the Secretary of State for Scotland, and others included Dr. W. A. Alexander, Sir Hector Hetherington, Dame Hilda Lloyd, Sir David Allan Hay, and Sir David K. Henderson. Professor David Campbell, president of the General Medical Council, in proposing the toast of "The Sister Corporations," said that the Royal Corporations had become exclusive of the general practitioner, and he doubted if this was necessary or wise. It had given rise to the demand for a new College. He suggested that if the Scottish Royal Corporations wished to fulfil their function in Scotland they should consider union, with the setting up of a Scottish College or Academy of Medicine.

Fellowships in Clinical Research

The Medical Research Council invites applications for a second series of Fellowships in Clinical Research, tenable at centres in the United Kingdom during the academic year 1952–3. These Fellowships are open to suitably qualified medical graduates who desire to prepare themselves for a career in clinical research. In general, it is intended that each Fellow appointed under the scheme should be given an opportunity, as part of his training for clinical research, to study methods of research in the basic subject most germane to his particular clinical interest.

The awards will be made for a period of one year in the first instance and will be renewable annually in approved cases up to a maximum of three years in all. Stipend will be at the rate of £850 per annum, rising by annual increments of £75 to £1,000 per annum, and in addition superannuation provision will be made (or continued within the National Health Service scheme, if applicable, by arrangement with the Ministry of Health and the Department of Health for Scotland).

Candidates for these Fellowships must be medically qualified and clinically experienced, and should preferably have worked for a period in a department in which clinical research was in progress. Applicants will be invited to submit their own proposals as to type and place of work, but the Council will be glad to advise successful candidates on the selection of suitable centres of study and to assist in placing them in departments or laboratories where the desired training and experience can be obtained.

Applications must be sponsored in each case by the head of the appropriate department in the candidate's university or medical school, and an undertaking will be required that a suitable academic post in a clinical department will be available to the candidate in that institution on satisfactory completion of the period of study under the Fellowship.

Forms of application for these Fellowships may be obtained from the Secretary, Medical Research Council, 38, Old Queen Street, London, S.W.1, with whom applications should be lodged as soon as possible, and in any event not later than March 1.

French Honour

The President of France has conferred upon Mr. R. W. Raven the Cross of Chevalier of the Legion of Honour.

Emergency Bed Service: Applications and Admissions

During the seven days ending December 31 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,015, of whom 93.1% were admitted.

Wills

The Medical Research Council is to receive about £80,000 to support research on cancer, under the will of Mr. John A. Hopps, of Leicester, a director of F. Hewitt and Son, Ltd., who publish the *Leicester Mercury* and other papers.

Sir Allen Daley, who retires from the post of M.O.H. to London County Council next month, will then become part-time associate health officer to Baltimore (Maryland) for four months and will lecture in several American schools of public health.

Professor W. Melville Arnott, of the University of Birmingham, who holds a W.H.O. Senior Travelling Fellowship, is visiting centres of medical education and cardio-respiratory research in the U.S.A. during the first quarter of 1952.

COMING EVENTS

British Association of Physical Medicine

The annual meeting of the British Association of Physical Medicine, 45, Lincoln's Inn Fields, London, W.C.2, will be held in London on Friday and Saturday, April 25 and 26.

Hunterian Oration

Dr. George Day will deliver the Hunterian Oration before the Hunterian Society at the Mansion House, London, E.C., on Monday, February 25, at 8.30 p.m.

Course on the Prostate

The Institute of Urology is holding an intensive short course on the prostate from January 14 to 25. In addition to daily lectures there will be operative sessions at St. Peter's and St. Paul's Hospitals each afternoon. Full details from the Secretary, Institute of Urology, Henrietta Street, London, W.C.2.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

OXFORD UNIVERSITY.—At Radcliffe Infirmary, Oxford, January 7, 8 p.m., "*The Use of Gelatinized Bone in the Repair of Skeletal Defects*," by Dr. Wilson A. Swanker (New York).

PHARMACEUTICAL SOCIETY OF GREAT BRITAIN, 17, Bloomsbury Square, London, W.C.—January 7, 7.30 p.m., "*The Nomenclature of Drugs*," by Mr. Frank Hartley, Ph.D., Ph.C., F.R.I.C.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—January 7, 5 p.m., "*Convergence, Convergence Abnormalities, and Heterophoria*," by Dr. T. H. Whittington.

Tuesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 8, 5.30 p.m., "*Sarcoid*," by Dr. R. M. B. MacKenna.

Wednesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 9, 5.30 p.m., "*X-ray Technique*," by Dr. C. W. McKenny.

PHYSICAL SOCIETY: COLOUR GROUP.—At Institute of Ophthalmology, Judd Street, London, W.C., January 9, 3.30 p.m., 64th science meeting. "*A Preliminary Report on Some Experiments on Tritanopia*," by Professor W. D. Wright; "*Light- and Dark-adaptation and the Perception of Colour*," by Mr. R. W. G. Hunt

SOCIETY OF CHEMICAL INDUSTRY: MICROBIOLOGY GROUP.—At Institution of Structural Engineers, 11, Upper Belgrave Street, London, S.W., January 9, 2.15 p.m., joint meeting of group with Society for Applied Bacteriology. Symposium on Disinfectants. "*The Bactericidal Action of Phenols in Aqueous Solutions of Soap*," by Professor H. Berry; "*A Substitute for the Rideal-Walker Test*," by Dr. P. Maurice; "*Some Factors Affecting the Bactericidal Action of Chlorine*," by Dr. L. A. Allen; "*The Antibacterial Action of Quaternary Ammonium Compounds*," by Mr. J. C. L. Resuggan; "*Some General Considerations Concerning the Activities of Disinfectants*," by Dr. S. E. Jacobs.

YORKSHIRE SOCIETY OF ANAESTHETISTS.—At Leeds General Infirmary, January 9, 8 p.m., *"The Heart and Anaesthesia,"* by Dr. B. G. B. Lucas.

Thursday

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, London, W., January 10, 8 p.m., *"Some Problems of Homosexuality,"* by Dr. Erwin Popper. Discussion to be opened by Dr. A. R. Redfern.

FACULTY OF HOMOEOPATHY, Royal London Homoeopathic Hospital, Great Ormond Street, London, W.C.—January 10, 5 p.m., *"Potentized Medicines for Use in Homoeopathy—Some Points on their Preparation and Care,"* address by Dr. W. R. McCrae.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY, The Union, University Avenue, Glasgow.—January 10, 7.30 p.m., Honorary Presidential Address by Professor Stanley Alstead.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 10, 5.30 p.m., *"Histopathology of Lichen Planus and Lichenoid Eruptions,"* by Dr. H. Haber.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool.—January 10, 8 p.m., ordinary meeting. *"Duodenal Ulcer,"* by Professor R. A. Gregory and Mr. James Moroney.

MEDICAL ART SOCIETY.—At 11, Chandos Street, London, W., January 10, 8 p.m., *"The Use of Pastels,"* talk and demonstration by Mr. J. K. Popham. He will afterwards criticize members' work.

ROYAL ARMY MEDICAL COLLEGE.—At Lecture Theatre, John Islip Street, London, S.W., January 10, 5 p.m., *"The Proper Sphere of Social Medicine,"* by Dr. Andrew Topping.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—January 10, 5 p.m., *"The Carcinogenic Process,"* Imperial Cancer Research Fund Lecture by Professor Alexander Haddow

Friday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—January 11, 5.30 p.m., *"Medical Photography,"* by the Institute Photographer.

OSLER CLUB.—At Medical Society of London, 11, Chandos Street, Cavendish Square, W.C., January 11, 7.45 p.m., History of Pneumonia Evening. *"Osler and Pneumonia,"* by Lord Horder; *"The Advent of the Sulphonamides,"* by Sir Lionel Whitby; *"The Changing Character of the Disease,"* by Sir Adolphe Abrahams.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—January 11, 8 p.m., *"Hypnotism and Medicine,"* by Mr. J. A. Gillies.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Revill.—On December 23, 1951, to Vivienne (formerly Macpherson), wife of Dr. Hugh Revill, of Snodland, Kent, a sister for Timothy.

Wyman.—On December 15, 1951, at Westminster Hospital, London, S.W., to Joan (formerly Beighton), wife of Dr. J. B. Wyman, a son.

MARRIAGES

Swan—Ede.—On December 19, 1951, at Edinburgh, Dr. Harold T. Swan to Dr. Elisabeth A Ede.

Williams—Thomas.—On October 27, 1951, at Machynlleth, Montgomeryshire, David Lloyd Williams, L.R.C.P.&S.Ed., L.R.F.P.S., to Gwyneth Thomas.

DEATHS

Brownlie.—On December 13, 1951, at his home in Hamilton, Lanarkshire, Andrew Brownlie, M.B., Ch.B., aged 75.

Busteed.—On December 18, 1951, at 31, Glenleigh Avenue, Bexhill-on-Sea, Sussex, John Hancock Busteed, L.R.C.P.&S.Ed., L.R.F.P.S., aged 85.

Fletcher.—On December 21, 1951, Nigel Corbet Fletcher, O.B.E., M.B., B.Chir., of 166, Haverstock Hill, London, N.W., aged 74.

Gibson.—On December 11, 1951, at Banbridge, Co. Down, Thomas Jordan Gibson, M.B., F.R.C.S.Ed., aged 57.

Hugo.—On December 24, 1951, at his home in Richmond, Surrey, Edward Victor Hugo, C.M.G., M.D., F.R.C.S., Lieutenant-Colonel, I.M.S., retired, aged 86.

Kelly.—On December 18, 1951, at Wareham, Dorset, William Davenport Crawley Kelly, D.S.O., M.B., B.Ch., Colonel, A.M.S., retired, aged 74.

McComas.—On December 13, 1951, at a hospital, Dorking, Surrey, Cyril Henry McComas, M.D.

Maskew.—On December 25, 1951, at The Wilderness, Langton Matravers, Dorset, Charles Henry Maskew, M.B., Ch.B., of 17, Weymouth Avenue, Dorchester, Dorset, aged 90.

Nathan.—On December 13, 1951, Nestor John Stanley Nathan, M.R.C.S., L.R.C.P., D.P.H., D.Obst.R.C.O.G., of Talke, Stoke-on-Trent, Staffs, formerly of Dewsbury, Yorks, aged 41.

Patterson.—On December 19, 1951, at a hospital, Edinburgh, William Berwick Ure Patterson, M.B., Ch.B., of 6, Magdala Crescent, Edinburgh.

Robinson.—On December 22, 1951, at Little Glebe, Fontwell, Arundel, Sussex, Charles Allen Robinson, M.B., B.Ch., D.M.R.E.

Smith.—On December 18, 1951, at Hemel Hempstead, Herts, Frederick Hugh Smith, M.B., Ch.B., formerly of Leeds, aged 56.

Square.—On December 18, 1951, William Holberton Square, L.R.C.P.&S. Ed.&L.M., J.P., of Bridge House, Leighton Buzzard, Beds, aged 91.

Strasheim.—On December 17, 1951, at Rondebosch Hospital, Capetown, South Africa, Pietrus Albertus Strasheim, M.B., Ch.B.

Sumpter.—On December 21, 1951, at Brancaster Staithe, Norfolk, Berners George Sumpter, M.B., M.R.C.S., aged 87.

Witney.—On December 15, 1951, Myfanwy Dyfed Witney, M.B., Ch.B., late of South India.

Any Questions ?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Seasickness

Q.—*How may seasickness best be prevented and treated?*

A.—L-Hyoscine hydrobromide is probably the best preventive against seasickness, although some people will be seasick whatever treatment they get and others can be prevented only from vomiting but continue to feel nausea. Hyoscine is best taken about one hour before exposure to motion, and it is less effective, though by no means ineffective, if taken five to ten minutes beforehand. It can be used to treat seasickness after vomiting has begun, but only if it is retained for a little while. The dose is 0.6 to 1 mg. This dose will cause drowsiness in some people, but other remedies also cause drowsiness, and so does untreated seasickness. The dose can be repeated at intervals of 6 to 12 hours up to a total of 2 mg. in 24 hours. If rough weather persists most people become adapted to the motion after about two days, but they soon lose this adaptation in calm weather or ashore and then treatment must be renewed. There is no evidence that seasickness remedies either hasten or delay the onset of adaptation.

Some antihistamine substances also prevent seasickness, but recent evidence suggests that they are less effective than hyoscine and, if anything, more toxic. Promethazine hydrochloride ("phenergan") is probably the best seasickness remedy among the antihistamine substances, and the dose is 25 mg. for adults, one to two hours before sailing.

Impulses from the vestibular apparatus are lessened if a person lies down, and people are less liable to seasickness when they do so.

All that has been said above applies also to other forms of motion sickness, although there are great differences in the way in which people respond to various types of motion.

Molluscum Contagiosum

Q.—*What treatment is recommended for molluscum contagiosum? Are antibiotics effective?*

A.—Individual lesions are easily removed with a small sharp spoon, and the base may then be cauterized with pure phenol or trichloracetic acid applied on a blunt stick. No anaesthetic is needed for this treatment and recurrences are unusual. It is perhaps as well, however, to warn the patient that further lesions may be "on the way" and may require treatment in two or three weeks' time. Recently there have been three reports from America of single cases of molluscum contagiosum treated apparently successfully with "aureomycin" (*Arch. Dermat. Syph.*, 1949, **60**, 629; *J. Pediat.*, 1949, **36**, 797; *Pediatrics*, 1951, **7**, 206).

It is of interest to note that although molluscum contagiosum seems to be auto-inoculable, case-to-case infection is not very common. Dr. B. B. Barrack, in Brisbane, has raised the question whether bird mites could be carriers of the virus.

Safe Period

Q.—*Where can I find information on the reliability of the "safe period"?*

A.—On p. 124 of the book *"Any Questions?"* The book can be obtained for 7s. 6d. (postage 6d.) from the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1.

Chronic Paronychia

Q.—*Can you recommend any treatment, apart from surgical, for chronic paronychia of the fingers?*

A.—Chronic paronychia is commonly due to pyogenic cocci or to monilia infection. With the former there is from time to time a discharge of pus; cultures from this may indicate a particular antibiotic, best given as general rather than local treatment. A wisp of cotton-wool saturated with pure carbolic may be packed into the sac, under the nail fold, by means of a matchstick the end of which has been tapered to a wedge shape. This is removed after an interval of 30 to 60 seconds, the object being to cauterize the infected walls of the sac. This may be followed by a fractional dose of *x* rays (120 to 150 r units, unfiltered, at 60 kV), and the procedure may be repeated once or twice at monthly intervals if necessary.

With monilia infection the nail fold is more swollen, "bolstered," and there is no pus, though it may be possible to express a cheese-like material. The use of aniline dyes in solution or in an emulsified ointment base together with *x*-ray treatment is usually effective.

In either condition there are invariably other factors demanding attention, such as a poor peripheral or "chilblain" circulation, debility or malnutrition, or unsuitable employment, particularly wet work and cooking.

Paronychia is sometimes due to ringworm fungus, when the nail is also involved, and the latter must be removed before the application of fungicides.

Calciferol and Boeck's Sarcoidosis

Q.—*Calciferol, 100,000 units daily, has been recommended for the treatment of Boeck's sarcoidosis. (1) For how long may this treatment be continued? (2) What toxic effects may occur, and what are the indications for interrupting therapy? (3) Are any biochemical or other tests useful in controlling treatment?*

A.—(1) The response of sarcoidosis to calciferol therapy is good. Necessary treatment may vary from a few months to a year or more, and relapses sometimes occur. Toxic manifestations are more readily provoked in patients with sarcoidosis than in those with lupus vulgaris, possibly because the patients tend to be older and the disease is more systemic. When calciferol is given by injection or in capsule, once a week in a dose of 600,000 i.u., toxic symptoms are less likely to occur than with tablets given daily in the same total weekly dose. It is unwise to give calciferol if there is any renal or cardiovascular disease.

(2) The earliest toxic symptoms are nausea, thirst, loss of appetite, abdominal pain, dehydration and pallor, headaches, and general malaise. Blood pressure and urine should be watched, and treatment should be interrupted if these symptoms arise or if albumin or sugar appear in the urine.

(3) Estimation of the blood urea is the most important guide to a toxic state. An increase in the diffusible calcium is often one of the first signs, but the investigation requires special facilities.

Toxic Reactions to P.A.S.

Q.—*(1) What toxic reactions may follow para-aminosalicylic acid (P.A.S.) therapy for pulmonary tuberculosis? (2) Which should be regarded as an indication for stopping treatment? (3) A patient treated for 28 days with 18 g. daily in divided doses (one day a week without treatment) developed a generalized erythema, which took a week to subside, but with no headache, nausea, vomiting, fever, or jaundice. Was this due to the P.A.S., and should treatment therefore be stopped?*

A.—(1) The most frequent and troublesome toxic reactions to P.A.S. are nausea, vomiting, and diarrhoea. Hypersensitivity to the drug, as shown by fever or rashes, together or separately, is not uncommon. Muscular weakness or heart irregularities, attributed to decrease in the serum potassium levels, have been described but are not often encountered. Jaundice may occur, but it has not been definitely demonstrated that this is attributable to P.A.S.; most of such cases have had injections of some kind and might be suffering from homologous serum jaundice. In animals, P.A.S. has an antithyroid action, but manifestations of hypothyroidism in patients having the drug are very rare and probably occur only in debilitated subjects or children given exceptionally large doses.

(2) Nausea, vomiting, and diarrhoea can often be minimized by taking the drug towards the end of a meal and by other simple measures. In a few cases it may be necessary to stop the drug for a day or two and then give gradually increasing doses. Exfoliative dermatitis, and possibly jaundice, are probably the only indications for stopping P.A.S. permanently. Other toxic symptoms may necessitate a temporary cessation.

(3) The generalized erythema in the case mentioned is probably due to hypersensitivity to P.A.S. From the way the question is put it appears that the rash subsided without the drug being stopped, in which case there is no necessity to stop treatment now. But if the rash subsided only after the drug was stopped, then the patient should be put back on treatment. If the symptom recurs, the drug should be stopped until the rash subsides and then the patient should be desensitized. An initial dose of 0.1 g. four times a day should be increased daily, successively to 0.5, 1, 2, 3, 4, and 5 g. Exceptionally, very sensitive patients require smaller initial doses or more gradual increases.

Anticoagulants and Cerebral Thrombosis

Q.—*What is the present status of the anticoagulant drugs in the treatment of cerebral thrombosis?*

A.—In general, anticoagulant drugs are not advised in cases of cerebral thrombosis, for the following reasons: (1) the differential diagnosis between intracerebral haemorrhage and thrombosis may in some cases be a matter of considerable difficulty; (2) it is recognized that a certain number of patients who have a cerebral thrombosis may have a cerebral haemorrhage a week or more after the thrombosis, probably due to alterations in the arterial wall in relation to the area of cerebral softening (*Lancet*, 1948, 2, 561); and (3) in a proportion of cases of cerebral softening no actual arterial thrombosis is found pathologically although there is atheroma and reduction of calibre in the relevant arteries.

Adrenal Ascorbic Acid

Q.—*What is the function of the ascorbic acid in the adrenal cortex?*

A.—The function of the ascorbic acid in the adrenal cortex is not known. Decrease in adrenal ascorbic acid after stimulation with adrenocorticotrophic hormone has led many to postulate that it is a precursor of adrenal steroids. On the other hand, the fact that the ascorbic acid content of other endocrine glands (i.e., pituitary and gonads) is high has been interpreted by others as an indication of non-specific metabolic hyperactivity.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors overseas should indicate on MSS. if reprints are required, as proofs are not sent abroad.

ADVERTISEMENTS should be addressed to the Advertisement Manager, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Britmedads, Westcent, London.*

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisecra, Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.